PREDICTORS OF SLEEP-WAKE DISTURBANCES IN BREAST CANCER SURVIVORS COMPARED TO WOMEN WITHOUT BREAST CANCER

Julie Lynn Elam

Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirements
for the degree
Doctor of Philosophy
in the School of Nursing,
Indiana University

June 2008

Accepted by the Faculty of Indiana University, in partial
fulfillment of the requirements for the degree of Doctor of Philosophy.

_____

Janet S. Carpenter, PhD, RN Chair

_____

Joan E. Haase, PhD, RN, FAAN

Doctoral Committee

_____

Susan M. Rawl, PhD, RN

February 7, 2008

_____

Silvia M. Bigatti, PhD

ACKNOWLEDGEMENTS

The following provided support for this study.

Dissertation committee

A special thank-you to the dissertation committee; Dr. Janet S. Carpenter, Dr. Joan Haase, Dr. Susan Rawl, and Dr. Silvia Bigatti. All members provided unwavering support and mentorship for this project.

Dataset sources

1. The American Cancer Society Quality of Life Study (#RSGPB-04-089-01-PBP, Dr. Victoria L. Champion PI).
2. Survey of Quality of Life in African American Women (NCI #R03 CA-097737 & Walther Cancer Institute Foundation, Dr. Kathy M. Russell PI).

Funding sources

1. NINR F31NR009890 Sleep-Wake Disturbances in Breast Cancer Survivors (Elam, PI) (2006-2008).
2. Society of Behavioral Medicine-Pre-doctoral Scholarship (2006).
3. American Cancer Society-Pre-doctoral Scholarship (2004-2008).
4. Walther Cancer Institute-Pre-doctoral Fellowship (2004-2006).
5. Oncology Nursing Society-Pre-doctoral Scholarship (2004).

ABSTRACT

Julie Lynn Elam

PREDICTORS OF SLEEP-WAKE DISTURBANCES IN BREAST CANCER SURVIVORS COMPARED TO WOMEN WITHOUT BREAST CANCER

Current evidence shows that sleep-wake disturbances are a persistent problem in women surviving breast cancer. The purpose of this study was to refine the knowledge regarding the incidence, prevalence, and predictive factors of sleep-wake disturbances in breast cancer survivors (BCS) compared to age-matched women without breast cancer (WWBC).

The cross-sectional, convenience-sample consisted of secondary data from BCS and WWBC who were recruited by two parent quality of life studies. Subjects were matched within +/- 5 years of age. The sample consisted of 246 BCS and 246 WWBC who were a mean age of 48 years old (SD=8.50), Caucasian (70%), employed (69%), married or partnered (76%), postmenopausal (59%), with a college education (56%), and with at least one concurrent medical problem (95%).

Results showed that BCS had more prevalent sleep-wake disturbances (65%) compared to WWBC (55%). The poorest sleepers were BCS, women with hot flashes, poor physical functioning, depressive symptoms, or with moderate or high levels of distress related to a life event. BCS had higher PSQI scores indicating poorer sleep quality and higher sleep disturbances compared to WWBC. Predictors of the severity of poor sleep quality and sleep disturbances were BCS, women with higher number of co-morbidities, women with hot flashes, lower levels of physical functioning, higher

depressive symptoms, and greater impact of a life event. Disease and treatment related factors did not predict poor sleep or sleep quality in BCS.

Sleep disturbances are a problem in long-term BCS. Knowledge of contributing factors provides useful information during clinical evaluations and treatment of BCS reporting poor sleep. Additional research is needed to determine the impact of poor sleep on quality of life and develop/test effective interventions for long-term BCS.

Janet S. Carpenter, PhD, RN Chair

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

Abbreviations	Term
BCS	Breast cancer survivor
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4^{th} edition
ECOG	Eastern Cooperative Oncology Group
EEG	Electroencephalography
GABA	Gamma-aminobutyric acid
GH	Growth hormone
HIPAA	Health Insurance Portability and Accountability Act
ICDS-R	International classification of sleep disorders-revised
IUPUI	Indiana University, Purdue University at Indianapolis
IUSCC	Indiana University Simon Cancer Center
IUSON	Indiana University School of Nursing
NREM	Non-rapid eye movement
PSG	Polysomnography
REM	Rapid eye movement
SCN	Supracarsmatic nucleic
SPSS	Statistical Package for the Social Sciences
WWBC	Women without breast cancer

CHAPTER ONE

INTRODUCTION

The following research focuses on predictors of sleep-wake disturbances in breast cancer survivors (BCS) compared to age-matched women without breast cancer (WWBC). The main objective was to provide information regarding factors that predict the occurrence and severity of sleep-wake disturbances that linger after treatment for breast cancer and how they differ from a group of age-matched women with no history of cancer. This research provides information regarding specific predictors of prevalence of poor sleep and severity of sleep disturbances in BCS. The conceptualization of sleep-wake disturbances provided a new and unique method of describing this problem and expanded on current theories of sleep research. Ultimately, information gained from this research will lead to targeted interventions that reduce potential negative consequences of sleep disruption and increase quality of life in various cancer populations.

Background and Significance

BCS represent a significant and growing population. Although breast cancer is the most common malignancy in women, with an estimated 182,460 new cases projected in 2008 (Jemal et al., 2008), the number of women who survive breast cancer continues to increase each year (Jemal et al., 2008). However, the five-year relative survival rates by stage at diagnosis are 98% for local stage tumors, 84% for regional stage tumors, and 27% for metastatic breast cancer (American Cancer Society, 2008). Because of the high survival rates, it has been reported that 2.2 million BCS are living in the United States (National Center for Chronic Disease Prevention and Health Promotion, 2004). The

decreased breast cancer mortality combined with (a) the relatively high five-year survival rates for local and regional stage tumors, (b) the aging of the United States population (U.S. Bureau of the Census, 1996), and (c) the potential medical issues encountered by survivors due to lingering treatment effects (Dow, Ferrell, Leigh, Ly, & Gulasekaram, 1996) suggest that BCS constitute an important population of interest. For this study, BCS are defined as women at least 1 year post completion of primary forms of treatment (surgery, chemotherapy, radiotherapy) and without residual breast disease.

Current evidence suggests that a significant proportion of BCS suffer from sleep-wake disturbances. Sleep-wake disturbances, defined as chronic disruptions in nighttime rest and/or wakefulness that result in physical, psychological, emotional, and/or social dysfunction, are reported at various times in the cancer trajectory (before, during, and after treatment). Studies are variable and show that 19-90% of BCS have chronic problems with sleep and wakefulness using self-report measures (e.g., Pittsburgh Sleep Quality Index) (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004; Berger et al., 2002; Berger et al., 2003; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Carpenter & Andrykowski, 1998; Clark, Cunningham, McMillan, Vena, & Parker, 2004; Fortner, Stepanski, Wang, Kasprowicz, & Durrence, 2002; Owen, Parker, & McGuire, 1999) or objective wrist actigraphy (Ancoli-Israel et al., 2005; Berger et al., 2002; Davidson, MacLean, Brundage, & Schulze, 2002; Engstrom, Strohl, Rose, Lewandowski, & Stefanek, 1999; Hunter et al., 2004; Lee, Cho, Miaskowski, & Dodd, 2004).

Consequences of sleep-wake disturbances in BCS can be immediate or delayed, affecting general physiological, social, and/or emotional functioning (Ancoli-Israel, Moore, & Jones, 2001; Anderson et al., 2003; Beck et al., 2004; Berger & Higginbotham,

2000; Bower et al., 2000; Carpenter et al., 2004; Davidson et al., 2002; Dow et al., 1996; Engstrom et al., 1999; Fortner et al., 2002; Koopman et al., 2002; Lee et al., 2004; Miaskowski & Lee, 1999; Okuyama et al., 2000; Roscoe et al., 2002; Savard & Morin, 2001). Decreased immune function related to lack of sleep can result in illness, infection, or mortality (Benca, 2005; Davidson et al., 2002; Fava, 2004; Shaver & Zenk, 2000; Thase, 2005). Social activities such as job performance, ability to do tasks at home, and socialization can also decrease (Anderson et al., 2003; Berger & Higginbotham, 2000; Lee et al., 2004; Miaskowski & Lee, 1999). Emotional/mental acuity and mood can decrease resulting in decreased mental alertness, depressive symptoms, emotional lability, anxiety, and distress (Anderson et al., 2003; Berger & Higginbotham, 2000; Lee et al., 2004; Miaskowski & Lee, 1999). These consequences are significant for the BCS population and have the potential to negatively impact overall quality of life (Deimling, Kahana, Bowman, & Schaefer, 2002; Ganz et al., 2002).

The reason sleep is such a salient topic for BCS is reflected by a powerful statement made during a qualitative exit survey following a behavioral intervention for hot flashes in a breast survivor (Carpenter, Neal, Payne, Kimmick, & Storniolo, 2007);

> "…It is the sleep (lack of) that is just killing every one of us…I really think that that's the part that critically needs to be looked at for most of us."

Although cancer patients in general are twice as likely to report sleep-wake disturbances, it is unclear what unique predictors are prevalent in long-term BCS. Studies have shown risk factors (Savard & Morin, 2001). The BCS literature shows a lack of conceptual clarity and variable prevalence rates of sleep-wake disturbances due to inconsistent terminology, inconsistent measures, and lack of longitudinal-comparative

studies. The result is evident by the lack of effective interventions specific for BCS with sleep-wake disturbances. Ultimately, additional descriptive work will provide guidance to develop effective interventions that enhance sleep, reduce negative consequences and improve quality of life during survivorship.

Statement of the Problem

The purpose of this study was to further refine the knowledge regarding the incidence, prevalence, and predictor factors of sleep-wake disturbances in BCS compared to age-matched WWBC. Based on the findings, the Psychobiological Model for Sleep-Wake Disturbances was refined.

Elements of the Problem

1. To compare the prevalence and severity of sleep-wake disturbances between BCS and age-matched WWBC.
2. To compare physiological, psychological, and environmental predictors of the occurrence and severity of sleep-wake disturbances in BCS and age-matched WWBC.
3. To refine the exploratory Psychobiological Model for Sleep-Wake Disturbances for BCS.

Theoretical Framework

The Psychobiological Model for Sleep-Wake Disturbances was the exploratory model for this study (Elam, unpublished). The model postulates relationships among variables (e.g., precipitating and perpetuating factors) thought to contribute to the occurrence of sleep-wake disturbances and negative outcomes in BCS using components of four related multi-disciplinary sleep models (described in Chapter Two) (Benca, 2005;

Berger & Walker, 2001; Blesch et al., 1991; Clark et al., 2004; Davidson et al., 2002; Espie, 2002; Hall et al., 1998; Hall et al., 2004; Harvey, 2002; Lacks & Rotert, 1986; Lee et al., 2004; Manber & Bootzin, 1997; Miaskowski & Lee, 1999; Owens & Matthews, 1998; Roscoe et al., 2002; Sadeh, Keinan, & Daon, 2004; Servaes, Prins, Verhagen, & Bleijenberg, 2002; Shaver & Zenk, 2000; Vena, Parker, Cunningham, Clark, & McMillan, 2004; Young, Rabago, Zgierska, Austin, & Laurel, 2003).

The Psychobiological Model for Sleep-Wake Disturbances in BCS postulates relationships among variables (e.g., precipitating, and perpetuating factors) thought to contribute to the occurrence of sleep-wake disturbances and negative outcomes in BCS (see APPENDIX A for critical attributes) (Benca, 2005; Berger & Walker, 2001; Blesch et al., 1991; Clark et al., 2004; Davidson et al., 2002; Espie, 2002; Hall et al., 1998; Hall et al., 2004; Harvey, 2002; Lacks & Rotert, 1986; Lee et al., 2004; Manber & Bootzin, 1997; Miaskowski & Lee, 1999; Owens & Matthews, 1998; Roscoe et al., 2002; Sadeh et al., 2004; Servaes, Prins et al., 2002; Shaver & Zenk, 2000; Vena et al., 2004; Young et al., 2003). The model was developed to enhance conceptual clarity for sleep-wake disturbances in the BCS population. The model uses components of the four models reviewed in Chapter Two adding specific factors related to BCS and is the proposed model for this research.

Visually and conceptually, the model proposes an interaction of potential predictors that contribute to the occurrence of sleep-wake disturbances in BCS. The bi-directional arrows among predictors indicate that one or several factors contribute to sleep problems. Specifics of these predictors are detailed later in this section.

The middle portion of the model explains the primary outcome of interest which is sleep-wake disturbance(s). Sleep is operationalized by subjective (Pittsburgh Sleep Quality Index) and/or objective (actigraphy or polysomnography) measures of sleep. These measures have been validated for use in the cancer literature. As the model is developed, additional serum tests might be added to provide a clinical diagnostic component to the model for further identification of specific etiology (e.g., thyroid dysfunction). The bi-directional arrows from sleep back to predictors are to explain how predictive factors can change over time. Thus, the precipitating factor(s) creating disturbances can be different than the perpetuating factor(s) (Espie, 2002). For example, a woman experiencing hot flashes could experience nighttime awakenings that disturb sleep. If the hot flashes subside, the nighttime awakenings can persist due to thoughts of concern of recurrence.

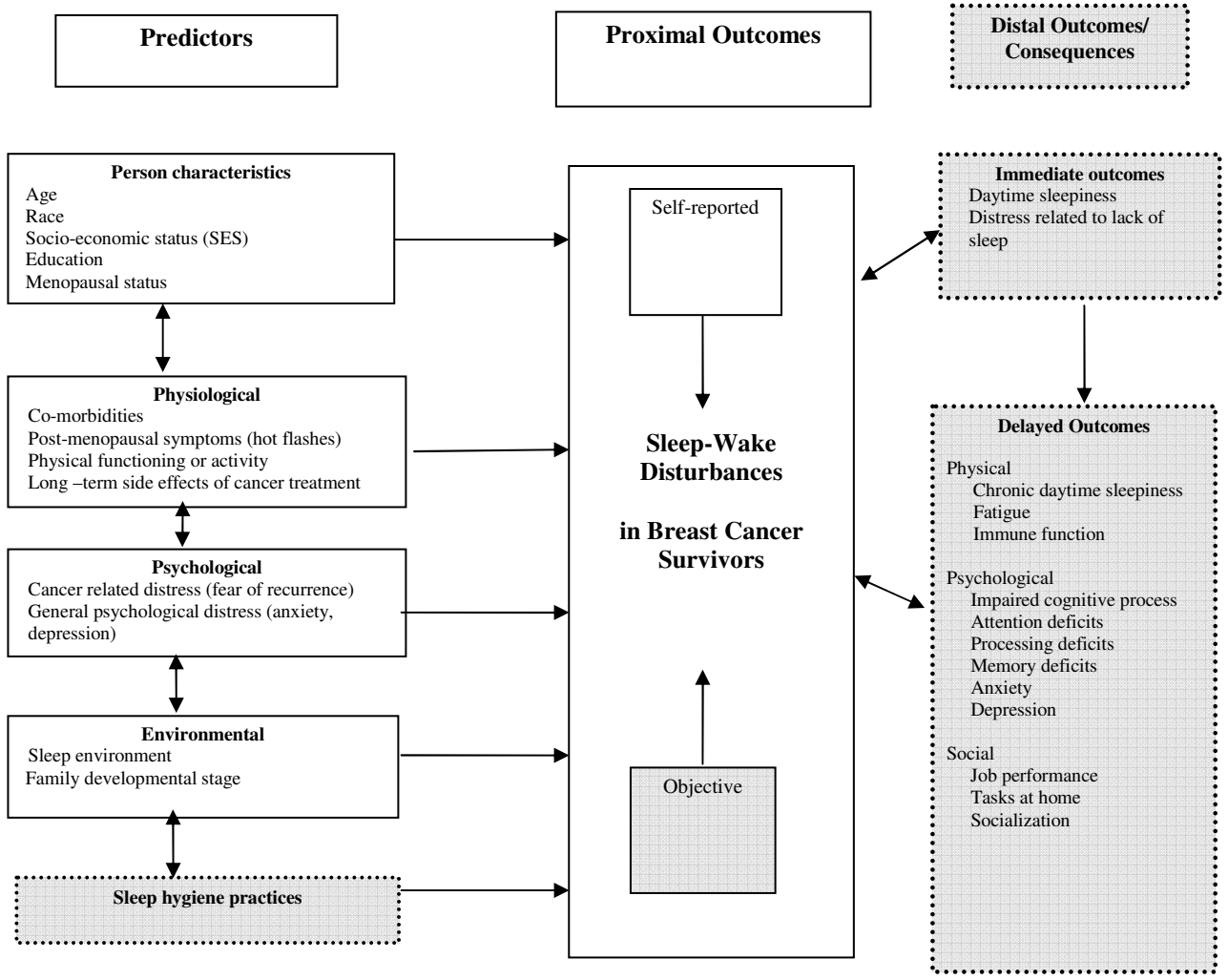
Lastly, the distal consequences of sleep-wake disturbances are classified as immediate and delayed. Conceptually, there is a bi-directional relationship between sleep-wake and resulting consequences to represent how immediate and delayed outcomes can be the result of and/or contribute to the continuation (perpetuation) of sleep-wake problems.

Immediate outcomes can include daytime sleepiness and distress related to the lack of sleep (Vena et al., 2004). Lack of sleep causes the body to put forth cues evidenced by feelings of daytime sleepiness and fatigue. These cues are often characterized by heaviness of the eyes during times of stimulus, heaviness of the body, and inability to stay awake during the day (Berger, 1998). As sleep-wake disturbances

progress over days, there is a tendency for the mind to become preoccupied about the need for sleep creating distress prior to bedtime (Espie, 2002; Harvey, 2002).

Delayed outcomes occur when sleep is disrupted over time. The models suggests that these outcomes are categorized as physiological (e.g., daytime sleepiness, fatigue), psychological (e.g., depression, anxiety), and social ramifications (e.g., loss of work time, disinterest in social engagements) that can negativity impact quality of life (Bleiker, Pouwer, van der Ploeg, Leer, & Ader, 2000). The outcomes of this model are shaded in grey denoting that this category will not be tested in this research study but rather addressed in future research. In addition, since this study used an existing dataset (see Chapter Three), the use of objective measurement such as wrist actigraphy was not feasible and will not be evaluated in this research study, thus also shaded in grey (see Figure 1).

Figure 1: Elam Psychobiological Model of Sleep-Wake Disturbances



Research Questions

This study investigated and compared sleep-wake disturbances and their predictors in BCS and WWBC. The following research questions were addressed.

1. Was there a difference in the prevalence of sleep-wake disturbances between BCS compared to age-matched WWBC?
2. Was there a difference in the severity of sleep-wake disturbances (defined by PSQI global scores and 7 component scores) between BCS compared to age-matched WWBC?
3. What were the physiological, psychological, and environmental predictors of poor sleep (defined by PSQI scores $\geq$5) in BCS and age-matched WWBC?
4. What were the physiological, psychological, and environmental predictors of the severity of sleep-wake disturbances (defined by PSQI global scores) of BCS and age-matched WWBC?

Table 1

Definitions of Key Terms Used in Sleep-Wake Literature

Key Terms	Definition
Breast cancer survivor (BCS)	Women at least 1 year post completion of primary treatment (surgery, chemotherapy, radiotherapy) and without residual breast disease.
Circadian rhythm	Daily fluctuation of physiological and/or behavioral functions such as sleep-wake linked to an internal 24-hour light/dark cycle. The rhythm can be increased or decreased when light cues are added or removed. Signals of time of day are called zeitgebers (time cues such as sunlight, noise, social interaction, or an alarm clock that entrains the internal clock).
Daytime sleepiness	The result of poor sleep; evidence by difficulty in maintaining an alert or awake state which causes rapid entrance into sleep when sedentary.
Electroencephalography (EEG)	Electrodes placed on the scalp to detect brain-wave activity- used in benchmark research to define the stages of sleep. EEG is now one component of polysomnography.
Homeostasis	The inherent tendency of an organism toward maintenance of physiological and psychological stability.
Insomnia	A type of sleep-wake disturbance related to the inability to fall asleep and stay asleep.
Non-rapid eye movement (NREM)	Non-rapid eye movement phases of sleep that constitute the first four stages of the sleep cycle.
Neurotransmitter	Specialized chemical messenger that sends a message from one nerve cell to another.
Polysomnography (PSG)	The objective recoding, analysis, and interpretation of multiple, simultaneous physiologic parameters of sleep-wake activity through a complex system of electrodes placed on the scalp, face and chest.
Rapid eye movement (REM)	Rapid eye movement phase of sleep, the dream phase.
Restless leg syndrome	A type of sleep-wake disturbance caused by the inability to relax the legs.

Key Terms	Definition
Sleep	The state of rest as opposed to the state of activity (wakefulness).
Sleep apnea	A type of sleep-wake disturbance characterized by repetitive episodes of decreased or absent breathing during sleep causing decreased blood oxygen levels.
Sleep duration (total sleep time)	The amount of time in bed spent in actual sleep.
Sleep efficiency	The % or proportion of time in bed that was spent in actual sleep (total sleep time/total time in bed).
Sleep hygiene	Behavioral practices that promote continuous and effective sleep (e.g., no caffeine 2 hours prior to sleep).
Sleep latency	The time in bed with lights out to the onset of the initial stages of sleep.
Sleep medicine	Refers to the discipline or specialty of sleep.
Sleep-wake disturbance	Chronic disruptions in nighttime rest and/or wakefulness that result in physical, psychological, emotional, and/or social dysfunction.
Translation	Integrating research findings (assessment practices and interventions) into clinical practice to maximize patient outcomes.
Wakefulness	State of alertness and activity.
Women without breast cancer (WWBC)	In lieu of using the term 'healthy women' to represent the age-matched control group, this group will be termed 'women without breast cancer' to avoid the assumption that BCS are not healthy.

Definitions for the above table were obtained from the following sources (American Sleep Disorders Association, 1994; Bowman, 2003; Bowman & Moshenin, 2003; Faruque, Bowman, & Sisson, 2003; Kerner, Rimer, & Emmons, 2005; Vena et al., 2004).

Summary

Sleep-wake disturbances are problematic in BCS. Due to the lack of knowledge regarding prevalence, severity, and predictors of this problem in BCS compared to WWBC, the following study evaluated the prevalence, severity, physiological, psychological, and environmental predictors of sleep-wake disturbances in BCS compared to age-matched WWBC.

CHAPTER TWO

REVIEW OF LITERATURE

Sleep is a restorative process essential for proper human functioning. Humans spend one-third of their entire lifespan in a state of nighttime sleep (Bowman & Moshenin, 2003). Disruptions in sleep have the potential to disrupt vital human processes such as immune and endocrine function. Sleep and wake are also linked to cognitive, behavioral, and environmental factors that contribute to sleep maintenance and quality. Because sleep-wake disturbances are so prevalent in BCS, knowledge of sleep physiology helps us to better understand potential etiologies of sleep-wake disturbances in this population. Therefore, the purpose of this chapter is to link the science of sleep research and sleep-wake disturbances in BCS. The chapter is divided into two parts and provides (1) an overview of sleep and (2) an overview of sleep in BCS. Since the topic of sleep is a multi-disciplinary topic, this chapter includes perspectives from medicine, psychology, and nursing.

Part I: Overview of Sleep

Part I of this chapter provides an overview of sleep essential for understanding why sleep is so important for normal human functioning. This discussion is divided into six sections; (a) sleep physiology, (b) classification of sleep and sleep disorders, (c) measurement of sleep, (d) negative consequences of poor sleep, (e) conceptual and theoretical aspects of sleep-wake, and (f) interventions for sleep-wake disturbances.

Sleep physiology

Sleep can be defined as a state of rest, as opposed to a state of activity (wakefulness) (Parker, Kutner, Bliwise, Bailey, & Rye, 2003). Sleep research began in the 20th century and resulted in a better understanding of sleep physiology, sleep problems, and the negative consequences of disturbed sleep (Bowman & Moshenin, 2003). Early research identified the stages of sleep using a device called the electroencephalogram (EEG) that evaluated wave inputs from the nervous system via electrodes that attached to the scalp (Aschoff, 1965; Dement & Vaughan, 2000; Purves et al., 2004). Researchers found that brain wave activity is distinctly different at various stages of sleep and wakefulness based on these neural inputs (Bowman & Moshenin, 2003). These benchmark findings provided the foundation for the current discipline of sleep medicine. When discussing the physiology of sleep, it is important to cover several topics. This section reviews the following; stages of sleep, neurobiology of sleep, circadian regulation of sleep, and homeostatic processes of sleep, including endocrine, thermoregulatory, immune function, and genetics.

Stages of sleep

Sleep begins with a non-rapid eye movement phase (NREM) and then transitions into a cyclic pattern of NREM and rapid eye movement (REM) sleep. Each cycle of NREM and REM sleep recurs approximately every 90 minutes, with the average cycle lasting 90-110 minutes (Aschoff, 1965; Bowman, 2003). Stages of sleep are often referred to as ‘sleep architecture’ to reflect the structure and timing of events (Bowman & Moshenin, 2003; Vena et al., 2004).

Non-rapid eye movement.

Non-rapid eye movement in adults is divided into four stages (stage 1-4). Each succeeding stage consists of progressively deeper sleep and higher arousal thresholds making it more difficult to awaken (Bowman, 2003; Miaskowski & Lee, 1999). The initial drowsiness experienced before sleep is considered stage I and reflected by increased EEG amplitude (height of wave) and decreased frequency (number of waves) (Ancoli-Israel et al., 2005; Aschoff, 1965; Aserinsky & Kleitman, 1953; Bowman & Moshenin, 2003; Krauchi & Wirz-Justice, 2001; Purves et al., 2004). Stage I progresses into stage II (light sleep) as reflected by further increases in amplitude and decreases frequency. Sleep spindles, (bursts of waves visible on an EEG), are noted with intermittent, high-frequency clusters of activity spikes lasting 1-2 seconds. These spindles reflect communications between the thalamic and cortical neurons in the brain. Stage I and II are easily disrupted because the body's threshold for arousal is low (Purves et al., 2004).

Stages III and IV are considered moderate to deep sleep. Stage IV is the deepest phase of sleep and also referred to as slow-wave sleep. Delta waves (one specific type of wave pattern on the EEG) are characteristic of stage IV where arousal is most difficult. At the end of stage IV sleep, EEG readings show marked changes in amplitude and frequency which signals the brain is entering the rapid eye-movement phase of sleep (Bowman & Moshenin, 2003).

Rapid eye movement.

The rapid eye movement (REM) phase of sleep is markedly different from the first, four stages of NREM. EEG readings show activity similar to wakefulness with

highly irregular amplitude and frequency waves. This unique stage of sleep, also known as the dream phase, remains a mystery. When deprived of REM, humans show minimal effects in normal functioning as stages I-IV are essential for maintenance of essential physiological processes (Purves et al., 2004). However, research has linked increased REM duration to depression symptoms and recently the target of sleep interventions such purposeful reduction of REM cycles (Savard, Simard, Ivers, & Morin, 2005a; Thase, 2005).

If one or more stages of NREM-REM cycles are disrupted, the body tries to recover those specific stages of sleep in the subsequent nights (Zee & Harsanyi, 2003). Thus, variability in nighttime sleep patterns is expected and normal for most individuals and typically resolves the next night (Espie, 2002). It is the constant disruption over time that results in negative consequences (Zee & Harsanyi, 2003).

Neurobiology of sleep

Sleep is controlled by a complex relationship between the central (brain and spinal cord) and peripheral nervous system (links rest of body to central system), and circadian rhythm functions (internal clock) (Guyton & Hall, 1997). The central and peripheral nervous systems work with the circadian rhythms within the body through complex circuits of neurons (signals) that produce changes in breathing, heart rate, and immune function during sleep.

Central regulation of the sleep-wake cycles involve inhibitory and excitatory signals to and from neural pathways (Moruzzi & Magoun, 1995; Purves et al., 2004). These pathways communicate information to the reticular activating system, cholinergic nuclei in the pons/midbrain, ventrolateral pre-optic nucleus, and areas of the thalamus.

Pathways are typically stimulated to cause wakefulness and inhibited for resting states (Purves et al., 2004).

The major inhibitory neurotransmitter in the central nervous system involved in sleep regulation is gamma-aminobutyric acid (GABA). Knowledge of central neurotransmitter action has evolved though the study of pharmacologic hypnotics that induce sleep. GABAnergic neurons, located on the basal forebrain and anterior hypothalamus, are released in response to the body's need for sleep. When the eyes are closed to induce sleep, GABA is produced and continuously released during NREM (Siegel, 2004). The function of GABA is to inhibit arousal functions within the basal forebrain, thus, deactivating the central mechanisms for wakefulness (Siegel, 2004). This deactivation is the result of GABA blocking neurotransmitters such as histamine, serotonin, and norepinephrine which are linked to arousal (Siegel, 2004).

As signals from the central nervous system are processed, messages are sent to the autonomic branch of the peripheral nervous system promoting physiological changes within the body. The autonomic system consists of nerve fibers that leave the brain and sacral portion of the spinal cord that are connected to blood vessels, glands, and other internal organs. During NREM, there is a reduction in the parasympathetic and sympathetic activity of the autonomic system causing decreased cardiopulmonary (e.g., heart function, breathing), skeletal muscular (e.g., postural tension, eye movements), core body temperature, and cognitive (e.g., memory functions) processes (Bowman & Moshenin, 2003; Purves et al., 2004). Conversely, during REM sleep, activity in the autonomic systems are highly activated even though some muscles are in a paralytic state (Vena et al., 2004).

Circadian regulation of sleep

In addition to the complex system of neurological functions, sleep is regulated by an internal circadian rhythm (Taheri, 2004). The following section will provide links between circadian function and normal homeostatic processes such as endocrine regulation, temperature regulation, and immune function. Information regarding the genetics of circadian rhythms will provide new links between genetic polymorphisms (variations in genetic codes) and sleep-wake disorders.

The circadian rhythm is the daily fluctuation of physiological and/or behavioral functions of a 24-hour light/dark cycle dependent on environmental cues (zeitgebers) (Aschoff, 1965; Borbely, 1982; Buysse et al., 1991; Claustrat, Brun, & Chazot, 2005; Jean-Louis, Kripke, Assmus, & Langer, 2000; Purves et al., 2004; Roscoe et al., 2002; Uchiyama et al., 2000). The circadian rhythm is a free running cycle dependent on cues such as light and dark (entrainment) that reset the clock every 23-24 hours.

Through studies of mammalian brain activity, researchers discovered the suprachiasmatic nuclei (SCN), now considered the pacemaker of the circadian rhythm in humans (Aschoff, 1965; Cermakian & Boivin, 2003; Moore, 1990; Purves et al., 2004). The SCN is dependent on zeitgebers to regulate the release of hormones to the neurological system (e.g., melatonin) thought to maintain sleep. The SCN is critical for sleep-wake circadian rhythmicity, thus, malfunction of the SCN or entrainment pathway can lead to random distributions of sleep cycles and frequent nighttime awakenings (Faruque et al., 2003; Moore, 1990). If these cues are removed, the body is unable to maintain the cycle causing disruptions in normal homeostatic processes.

Homeostatic processes

Endocrine function.

The human endocrine system is linked to circadian function through the production and release of neuroendocrine hormones such as growth hormone, cortisol, estrogen, thyroid stimulating hormone, glucose, and estrogen (Faruque et al., 2003). Disrupted circadian cycles result in abnormal production and release of these hormones which can result in organ failure (e.g., kidney or thyroid) (Rich et al., 2005; Vena et al., 2004). The importance of these hormones is outlined below.

Growth hormone (GH), responsible for growth and cell repair (Merriam-Webster Inc., 1991), is secreted from anterior pituitary during the first few stages of sleep (Faruque et al., 2003). The secretion of GH is thought to promote NREM sleep and new cell growth. As humans age, GH secretion decreases in response to the body's diminished need for new cell growth (compared to a growing adolescent). In addition, lower levels of GH over time decreases NREM as reflected by the decreased sleep experienced by the aging population (Faruque et al., 2003).

Cortisol, a hormone produced in the adrenal cortex, is secreted during the late phases of sleep. Cortisol has several important functions such as synthesizing carbohydrates from proteins for maintenance of blood glucose levels necessary for normal endocrine function. Sleep-wake cycles are a timing mechanism for cortisol release, thus, if sleep is erratic, cortisol levels significantly increase and result in nighttime awakenings (Sephton, Sapolsky, Kraemer, & Spiegel, 2000). It remains unclear if altered cortisol indicates poor sleep patterns or if they are the result of poor sleep.

The thyroid, a gland located beneath larynx, produces a hormone called thyroid stimulating hormone that regulates growth and metabolism (Guyton & Hall, 1997). Thyroid function also decreases with aging (especially in women) resulting in chronic hyper- or hypothyroidism. Abnormal thyroid function has been linked to sleep-wake disturbances due to heightened metabolism rates that cause increased alertness (Faruque et al., 2003). Sleep disturbances re a consequence or outcome of abnormal thyroid function. For example, individuals with hyperthyroidism are prone to obstructive sleep apnea because the gland becomes enlarged (goiter) causing pressure on the larynx during sleep.

Estrogen has been implicated in sleep and thermoregulatory processes (see next sub-section), although its role is largely unclear (Leibenluft, 1993; Scharf, McDannold, Stover, Zaretsky, & Berkowitz, 1997; Schiff, Regestein, Schinfeld, & Ryan, 1980). Estrogen production is synchronized with circadian cycles and secreted during NREM sleep (Empson & Purdie, 1999). Researchers suggest that increases in estrogen lengthen total sleep time, decrease sleep latency, and improves sleep efficiency (Schiff et al., 1980). Because estrogen is an important hormone in women, studies typically evaluate estrogen's role in sleep comparing pre-and postmenopausal subjects. Schiff et al. (1980) compared postmenopausal women who were given conjugated estrogen therapy vs. placebo to evaluate differences in adrenal and pituitary hormone function during their sleep. Results indicated that compared to the placebo group, those on estrogen therapy had significant increases in total REM sleep and significantly shorter sleep latency (time to fall asleep) equating to increased sleep efficiency. This provides support that estrogen plays a role in the process of sleep (Schiff et al., 1980).

Thermoregulation.

In addition to endocrine function, sleep helps regulate normal body temperature. Thermoregulation is the internal processes (e.g., shivering, sweating) that maintains a stable internal temperature (Faruque et al., 2003). Thermoregulation during sleep regulates the body's metabolic rate needed to sustain cellular function. There is a circadian temperature rhythm activated during sleep that assists in thermoregulation. During sleep, this circadian rhythm lowers core body temperature during NREM. However, during REM temperature regulation is inhibited and an entry point for sleep-disturbances such as menopausal hot flashes (Siegel, 2004). The inability to maintain a stable nighttime core temperature due to decreased NREM can cause frequent awakenings and poor, fragmented sleep.

Immune function

Cytokines, regulatory proteins of the immune system, are synthesized and released for destruction of abnormal cells during illness and trauma. Cytokine (e.g., tumor necrosis factor, interleukins) production requires an increased amount of sleep for adequate disbursement throughout the body (Guyton & Hall, 1997). The drive for sleep during illness is reflected by the body's desire for increased NREM sleep (Faruque et al., 2003). In chronic illness, sleep duration and quality are not always optimal due to treatment side effects (e.g., nausea vomiting), pain, or other illness-related factors. Although studies show that healing is compromised, the long-term effects of chronic sleep problems and immune function remains under-reported (Dogan, Ertekin, & Dogan, 2005).

Genetics of sleep

There is a genetic link between circadian function and sleep. This link was first discovered by researchers through examination of abnormal circadian rhythms in fruit flies (Konopka & Benzer, 1971; Purves et al., 2004). Ten unique genes manufactured during the day and nighttime have been identified and labeled as clock genes (B-mal 1, Period (Per), Timeless (Tim), Casein Kinase 1 (CK1), Cryptochrome (Cry1 and Cry2)) (Taheri, 2004). Polymorphisms in clock genes have been linked to restless leg syndrome, obstructive sleep apnea, and narcolepsy in adults. This exciting new area of research will produce important links in future identification of additional polymorphisms and other types of sleep-wake disturbances in various populations.

In sum, sleep and wake is a system of physiological stages linked by neurobiological, circadian, and homeostatic processes. Sleep occurs in series of stages dependent on various neurological, circadian, endocrine, thermoregulatory, immune, and genetic functions. The complexity of sleep-wake physiology provides a foundation for further discussion of how disruptions in sleep can cause potential negative outcomes.

Classification of sleep and sleep disorders

The following will review the types of sleep-wake disturbances and two common categories of diagnostic criteria used in research and clinical practice. Disparities among disciplines are noted regarding which terms and criteria should be used in clinical and research settings.

Types of sleep-wake disturbances

Generic categories of sleep-wake disturbances include; (a) decreased hours of sleep (sleep duration or total sleep time), (b) increased number of minutes to fall asleep

(sleep latency), (c) number and length of nighttime awakenings (sleep disruptions), (d) quality of perceived sleep (sleep quality), (e) amount of time in bed spent asleep (sleep efficacy), and (f) inability to function fully during the day without naps (daytime dysfunction) (Berger, 1998; Buysse et al., 1989; Miaskowski & Lee, 1999). These disturbances can occur alone or in combination affecting overall sleep quality and daytime function (Ancoli-Israel et al., 2003; Buysse et al., 1989; Espie, 2002; Fry, 1987). Although useful for research, generic sleep categories are not adequate for clinical diagnosis.

Diagnostic criteria

Diagnostic criteria used to diagnose sleep-wake disturbances are variable. Common etiologies in healthy populations are obstructive sleep apnea, insomnia, restless leg syndrome, and excessive daytime sleepiness. The two main categories for the clinical diagnosis of sleep disorders are listed in detail below.

ICDS-R categories.

Sleep and wake problems can be diagnosed using three International Classification of Sleep Disorders (ICDS-R) categories: dyssomnias, parasomnias, and mental/neurological/other medical disorders (American Sleep Disorders Association, 1994). Dyssomnias involve difficulty initiating sleep (sleep latency), maintaining sleep (sleep disruption, sleep duration), and/or excessive sleepiness (daytime dysfunction). Parasomnias are abnormal behaviors and/or sensations during sleep (sleep disruptions) such as sleepwalking, nightmares, and/or sleep talking. The third category is a catch-all for all other types of sleep-wake disturbances including mental (e.g., anxiety), neurological (e.g., dementia, Parkinsonism) and/or other medical disorders (e.g.,

nighttime cardiac ischemia) (American Sleep Disorders Association, 1994; Vena et al., 2004).

DSM-IV categories.

Sleep-wake disturbances can also be diagnosed using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for primary and secondary insomnia (American Psychiatric Association, 1994). Primary insomnia refers to difficulty initiating and/or maintaining sleep (sleep latency, sleep duration) or non-restorative sleep for at least 1 month resulting in feelings of distress (daytime dysfunction) (American Psychiatric Association, 1994; Thase, 2005). Secondary insomnias are due to psychiatric (e.g., depression), neurological (e.g., restless leg syndrome), and/or medical contributors (e.g., obesity) to sleep disturbances (American Psychiatric Association, 1994). Primary or secondary insomnia can be transient (sporadic-days), acute (less than 3 weeks), or chronic (more than 3-4 weeks).

There is currently no agreement among researchers as to which classification system is more precise. Use is highly dependent on the discipline in which the sleep disturbance is being evaluated. Classification of sleep disorders is dependent on the specialty performing the clinical evaluation. The ICDS-R originates in the fields of medicine and psychiatry whereas the DSM-IV is derived from psychology. Some nurse researchers suggest solely using the ICDS-R, but this remains merely a suggestion and its use continues to be inconsistent within the nursing literature (Vena et al., 2004).

Measurement of sleep-wake disturbances

Proper identification of sleep-wake disturbances can be accomplished through subjective and objective measures. Both types of measures have been validated in various

populations including BCS. Measurement is stated to be one of the major challenges of sleep research due to the various methods used to capture sleep variables (Berger et al., 2005). The following sections summarize common objective and subjective measurements of sleep-wake disturbances.

Objective sleep

The gold standard of sleep measures is polysomnography (PSG). This tool provides understanding of both normal and disturbed sleep through a collective process of monitoring and recording physiologic data (Keenan, 2003). Subjects spend 1-2 nights in a controlled sleep lab managed by certified sleep technicians. The process includes the attachment of electrodes to the face, neck, and chest to detect nervous system activity (Keenan, 2003). These currents are transmitted as waveform tracings evaluated for initiation and progression of sleep cycles. Three separate waveform tracings are evaluated: electroencephalogram (EEG) (brain waves), electrooculogram (eye movements), and electromyogram (muscle tension) (Bowman & Moshenin, 2003). Results provide clinicians with the timing of sleep cycles and disruptions to determine underlying etiologies of sleep disturbances (Keenan, 2003). Although polysomnography is the gold standard of sleep, it is more expensive and time consuming compared to less invasive measures such as wrist actigraphy and self-report (Kushida et al., 2001).

Wrist actigraphy has been used as a sensitive objective measure of sleep in both cancer and healthy populations (Ancoli-Israel et al., 2003; de Souza et al., 2003; Kushida et al., 2001; Means, Edinger, & Husain, 2002; Wilson, Watson, & Currie, 1998). The device is worn on the non-dominant wrist, typically for 3-7 days (Ancoli-Israel et al., 2003; de Souza et al., 2003; Hauri & Wisbey, 1992; Littner et al., 2003). The device

contains an accelerometer that is able to sense any motion with a minimal force greater than 0.01g (Mini Mitter Company Inc., 2003). The sensor integrates the speed and degree of motion, which produces an electrical current that varies in magnitude. Studies show a high correlation between wrist actigraphy and polysomnography in the assessment of total sleep time and number of nighttime awakenings in healthy individuals, with correlations of 0.95 for sensitivity, 0.36 for specificity, and 0.80 for accuracy (Kushida et al., 2001). These correlations have been replicated in various other validation studies (Ancoli-Israel et al., 2003; de Souza et al., 2003).

Subjective sleep

There are numerous subjective measurements of sleep variables (e.g., quality, latency, duration). The following discussion will focus on the common assessment of sleep quality in the cancer population providing brief overviews of the other options for sleep measurement (Carpenter et al., 1998; Carpenter, Johnson, Wagner, & Andrykowski, 2002; Savard & Morin, 2001; Vena et al., 2004).

First, the Pittsburgh Sleep Quality Index (PSQI) was designed for use in clinical populations as a simple and valid assessment of sleep (Buysse et al., 1989). The tool contains 19-items that produce a global sleep quality score based on 7 component scores: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications, and daytime dysfunction. PSQI items use varying response categories including Likert-type responses. Responses are based on the prior month's habits. Psychometric properties of the PSQI such as content validity and internal consistency reliability have been widely supported in a variety of populations,(Gentili, Weiner, Kuchibhatla, & Edinger, 1995; Pasternak et al., 1994; Tiffin, Ashton, Marsh, &

Kamali, 1995) including healthy individuals (n=52; α=0.83) (Buysse et al., 1989) and BCS (n=102; α=0.80) (Carpenter & Andrykowski, 1998).

A second questionnaire receiving more attention in the cancer literature is the Insomnia Severity Index (ISI), a tool recently developed to detect insomnia in cancer patients (Savard, Savard, Simard, & Ivers, 2004). This 7-item questionnaire evaluates the perceived severity of insomnia over the past 2 weeks. Items are scored using a Likert-type scale with 5 response options (0=not at all to 4=very much). Total scores are obtained by summation of the 7-items for scores ranging from 0 to 28 (Savard, Savard et al., 2004). Higher scores indicate greater perception by subjects of insomnia severity. Internal consistency-reliability and content validity have been established in healthy individuals (n=145 α=0.74) and cancer patients (n=1634; α=0.90) (Bastien, Vallieres, & Morin, 2001; Savard, Savard et al., 2004). The recent validation of this tool will provide additional means to screen for clinical insomnia in cancer patients.

Other questionnaires that assess sleep quality include the Verran and Snyder-Halpern Sleep Scale (Snyder-Halpern & Verran, 1987) and the Sleep Timing Questionnaire (Monk et al., 2003). Both measures provide frequency and severity scores for sleep disturbances. Although both are stated to be valid and reliable measures, they have not been validated in cancer populations, and, thus, are rarely used in cancer research.

Sleep diaries are often used to determine time to bed, time awake, perceived sleep quality, pre-sleep routines, and napping. The Karolinska Sleep Diary (Akerstedt, Hume, Minors, & Waterhouse, 1994), the Sleep Log (Spielman, Nunes, & Glovinsky, 1996), and the Pittsburgh Sleep Dairy (Monk et al., 1994) have similar formats that include either 1

or 7 day assessment of sleep. Sleep diaries are often combined with the use of wrist actigraphy to determine the time to bed and time awake for data analysis.

In sum, there are numerous measures of sleep that are validated for use. However, there is one major problem with the use of both subjective and objective measures. Data shows that the correlation between subjective and objective measures is variable (Harvey, 2002; Harvey & Espie, 2004; Hauri & Wisbey, 1992). It has been noted that self-reported sleep is perceived to be much worse compared to PSG or actigraphy findings (Ancoli-Israel et al., 2003; Elam & Carpenter, 2004a; Savard et al., 2005a). Without consistent measurements of sleep, the scope of negative outcomes that results from poor sleep are uncertain. In addition, it remains unclear whether the disconnect between subjective and objective measures impacts the efficacy of interventions.

Negative outcomes of sleep-wake disturbances

Once the specific sleep-wake disturbance has been classified and measured, it is important to determine how this disturbance is impacting the individual's health. The occurrence of sleep-wake disturbances can negatively impact physical and psychosocial well-being (Benca, 2005; Savard & Morin, 2001). Although negative consequences can be acute or chronic depending on the chronicity of sleep disturbances, research typically focuses on the long-term problems associated with disturbed sleep. The following will provide a discussion of; (a) physiological outcomes, (b) psychosocial outcomes, and (c) measurement of negative outcomes of sleep-wake disturbances.

Physiological outcomes

As noted above, fragmented sleep can lead to disruptions in homeostatic processes thereby leading to the exacerbation of disease, inability to heal, and altered

metabolic and endocrine function. For example, essential cytokines required for immune function can be compromised due to fragmented sleep (frequent awakenings) thereby compromising the ability to heal. Although these effects may not be immediate, they require close attention during clinical evaluation to prevent co-morbid conditions.

Psychosocial outcomes

In addition, psychosocial consequences from chronic sleep-wake disturbances include depression, anxiety, decreased in job performance, lack of desire for socialization, inability to perform activities of daily living, and cognitive impairments resulting in poor quality of life. These issues are typically related to daytime sleepiness which creates overwhelming fatigue and increased desire for sleep (Sateia & Nowell, 2004). Lastly, the social burden of sleep problems has gained increased interest (NIH State of the Science Panel, 2005). Consequences of chronic sleep-wake disturbances not only impact the person, but create a public health burden. There are few reports of large population studies regarding the economic impact of missed work days and job related disability due to sleep-wake disturbances (NIH State of the Science Panel). Future research is needed to address these issues and further expand our knowledge of the overall impact on society.

Measurement of negative outcomes

There are numerous measurements of negative outcomes. Such measurements include physical functioning (e.g., Medical Outcomes Short Form-36) (Ware & Sherbourne, 1992), psychological status (e.g., Center for Epidemiologic Studies Depression Scale) (Radloff, 1977), cognitive function (e.g., Mini Mental State Examination) (Folstein & Whitehouse, 1983) and social function (e.g., Functional

Outcomes) (Weaver et al., 1997). In addition, there are serum blood tests that are helpful to identify endocrine (e.g., thyroid stimulating hormone) and immune (e.g., cytokine assays) dysfunction during clinical evaluations of sleep (Chernecky & Berger, 2004). Future technology will undoubtedly produce methods of serum genetic testing that are readily available in the clinical setting that are now reserved for clinical research labs. Together, self-report and serum measurements provide crucial information regarding clinical and quality of life outcomes that have the potential to direct effective interventions.

Conceptual and theoretical aspects of sleep research

In research, underlying conceptual and theoretical clarity is essential to understand the problem under investigation. The following discussion provides a synthesis of: (a) conceptual terminology; (b) four theoretical sleep models; and (c) limitations of each model.

Theoretical models provide statements of relationships between concepts that explain or predict a certain phenomena (Polit & Hungler, 1999; Reed, Shearer, & Nicoll, 2004; Walker & Avant, 2005). Concepts within the theory provide labels, categories, or selected properties to be studied (Reed et al., 2004). The structure of the model ties together these relationships that should be operationally defined through validated measure (Polit & Hungler, 1999, Reed, 2004 #648).

Conceptual terminology

Predictors, also referred to as contributing factors, help describe the reason or reasons sleep-wake disturbances occur. Predictors of sleep-wake disturbances have been categorized in the literature as predisposing, precipitating, and perpetuating factors, each

of which will be discussed in detail below (Davidson et al., 2002; Espie, 2002; Fortner et al., 2002; Harvey, 2002; Spielman, Caruso, & Glovinsky, 1987; Spielman et al., 1996).

Predisposing factors.

Predisposing factors are individual differences that contribute to the onset of sleep-wake disturbances. Predisposing factors include; (a) age, (b) gender, (c) education status, (d) socioeconomics, and (e) pre-existing psychiatric disorders (e.g., depression, anxiety) (Ancoli-Israel et al., 2001; Clark, Flowers, Boots, & Shettar, 1995; Clark et al., 2004; Crandall, Petersen, Ganz, & Greendale, 2004; Espie, 2002; Lin, Ng, Chen, Hu, & Chen, 2005; Rosenthal, 2003; Vena et al., 2004). Because these are known factors that contribute to sleep-wake disturbances, they are often controlled for during statistical analysis.

Precipitating factors.

Precipitating factors contribute to the initial start point of sleep-wake disturbances (Espie, 2002; Harvey, 2002; Savard & Morin, 2001; Spielman et al., 1987). Precipitating factors can be physical, psychological, environmental, and/or sleep hygiene practice (pre-sleep routines) problems. Physical factors include pain, co-morbid conditions (e.g., heart and lung disease) and medication side effects that disrupt sleep. Co-morbid conditions such as heart and lung disease are often related to sleep apnea and frequent nighttime awakenings (Savard & Morin, 2001). Research suggests that lack of sleep often precedes the onset of heart and lung disease because of poor sleep. Furthermore, the medications taken for illness-related problems can disrupt the sleep cycle.

Common psychological illnesses associated with disturbed sleep are depression and anxiety disorders. Conversely, depression and anxiety have also been noted to be

consequences of sleep disorders. Due to the complexity of these psychological co-morbidities it is challenging to determine the trajectory (onset, diagnosis, and treatment) of insomnia related to the trajectory of other complex psychological disorders.

Environmental factors can influence sleep and include factors such as room temperature, noise, bedding, companion sleep, and/or child-rearing responsibilities (O'Connell, 2005). Environmental factors are rarely evaluated and it is unclear how they contribute to the occurrence and severity of prolonged sleep-wake disturbances. Sleep hygiene practices are often combined with environmental factors, and are the routine behaviors performed by an individual before bedtime such as reading, watching television, eating, smoking, drinking caffeine and/or alcohol, and exercising before bedtime (Cheek, Shaver, & Lentz, 2004). Because these practices are known to contribute to sleep-wake disturbances and can be modified, they have great potential as interventions to manage or reduce sleep-wake disturbances.

Perpetuating factors.

Perpetuating factors are factors that contribute to the continuation of sleep disturbances over time (Espie, 2002; Harvey, 2002; Savard & Morin, 2001; Spielman et al., 1987). Certain sleep models propose that precipitating factors can become perpetuating factors when sleep is disrupted over several nights. However, perpetuating factors can be different from those that contribute to the initial onset and also from physical, psychological, environmental, and sleep hygiene practices. It is difficult to differentiate the first occurrence of sleep-wake disturbances from subsequent occurrences (e.g., we cannot study sleep-wake disturbances before they occur to truly understand precipitating) since factors that precipitate the disturbances can be different from those

factors that perpetuate or continue the problem (e.g., stress). Therefore, precipitating and perpetuating factors are often discussed together.

Theoretical models of sleep

The above terminology is often used in current theoretical models of sleep. The following will address the critical attributes of four common models used in sleep research (see APPENDIX A). These models are based on physiological, cognitive, or bio-behavioral perspectives of sleep, wake and sleep-disturbances. Although the models provide useful perspectives regarding sleep, there are limitations to general use in research.

Physiological model.

The Two-Process Model of Sleep attempts to explain the physiological basis of sleep (Borbely, 1982; Borbely & Achermann, 1999). The model states that sleep and wakefulness are maintained by a set of neuroendocrine and hormonal balances essential to physical and mental functioning. Sleep is stated to be the physiological process regulated by: (a) the homeostatic processes that mediate the rise of sleep propensity during wake and dissipation of sleep propensity during sleep (Process S), and, (b) the circadian process (Process C) which determines alterations of high and low sleep propensity that is independent of prior sleep-waking (the timing to sleep and wakefulness) (Borbely, 1982; Borbely & Achermann, 1999). Furthermore, sleep is a balance of the autonomic nervous system (increased parasympathetic activation and decreased sympathetic drive), actions of the hypothalamic-pituitary-adrenal axis, and homeostatic sleep drive (Process S) and circadian sleep-wake rhythms (Process C) (Lee-Chiong, 2004).

Construct validity of the relationships among concepts of the model has been established and it is the predominate model used in fields of medicine and nursing (Berger et al., 2005; Clark et al., 2004; Vena et al., 2004). Although the two process model provides explanations for relationships among physiological sleep-wake processes (Borbely, 1982), it does not address how these disruptions lead to negative quality of life outcomes.

Cognitive model of insomnia.

The cognitive model presented by Harvey (2002) provides a framework for the interaction of sleep and cognitions (thoughts). The model was developed to explain characteristics between sporadic and chronic insomnia. The model suggests that people with insomnia experience unpleasant, intrusive thoughts or worry during pre-sleep (lying in bed) (Harvey, 2002). The entry point or initiation phase of the model is attributed to excessive thoughts about sleep and how the lack of sleep might impact health and daytime functioning (e.g., work performance). Positive thoughts can also lead to decreased sleep and can often turn negative when sleep does not occur. When excessive worries or intrusive thoughts (ruminations) persist, the onset of sleep is delayed due to physiological and emotional responses to stress. After the initiation phase of sleep disturbance, the mind continues to reevaluate surrounding stressors and thoughts and either continues or extinguishes these thoughts allowing for the onset of sleep (Harvey, 2002).

Harvey suggests that individuals overestimate the extent of perceived sleep deficits and daytime dysfunction. Distortions of perceived sleep create a positive feedback creating additional anxiety and erroneous beliefs regarding sleep.

The result is further negative thoughts before bed and continued disrupted sleep. In addition to nighttime cognitions, the model states daytime thoughts have an equivocal emphasis on negative cognitions. Daytime thoughts tend to focus on the need for better sleep in the upcoming night and inability to stay awake during the day.

Although this cognitive model provides relationships between cognitions and sleep disturbances there are several limitations. First, the model lacks validation with empirical research to support construct and content validity. Second, the model lacks inclusion of physiological, co-morbid conditions that can negatively impact sleep such as thyroid dysfunction. Third, because the model is specific for insomnia, it may not explain other types of sleep disturbances.

Psychobiological models.

The first multidimensional model of chronic insomnia provided interactions between predisposing, precipitating, and perpetuating factors of insomnia (Spielman et al., 1987). These factors were used to explain the evolution of insomnia and how individual differences contribute to the initiation of disturbed sleep. People with heightened arousal states (wake up easily) are typically poor sleepers (do not maintain normal sleep stages) and they often have precipitating factors such as anxiety, depression, and stress. As the lack of sleep continues, perpetuating factors of frustration and agitation about the inability sleep, contributes to further cognitive and physiological arousal, thus, further sleep disruptions. Maladaptive strategies include increased time to fall asleep, anxiety about daytime performance, and progression of psychological disorders such as anxiety and depression (Spielman et al., 1987). The unique contribution of this model

was the combination of biological interactions (arousals) with psychological factors of stress.

The major limitation of this model is inability to translate into various research settings since it focuses solely on aspects of chronic insomnia. The model proposes some relationships among psychobiological factors related to poor sleep, but does not explain how other disturbances such as restless leg syndrome and sleep apnea fit into this model. A second limiting factor is the lack of available statistical validation of the model which limits our knowledge of whether the concepts are statistically relevant in other research settings.

Espie (2002) developed a Psychobiological Model of Sleep Inhibition which combines biological (circadian function) and psychological (affect, cognitions and behaviors) factors that directly affect sleep and daytime functioning. The model postulates that chronic sleep disturbances are a function of precipitating and perpetuating factors that interfere with the automaticity and plasticity (night to night variations) of normal homeostatic and circadian sleep. Variations in sleep are expected but typically resolve when a restful night's sleep is experienced. Espie focuses on those sleepers that are unable to return back to a normal sleep pattern after disrupted sleep leading to daytime dysfunction. Poor sleepers then identify changes in sleep as a function of a progressive and serious sleep problem leading to further loss of sleep (Sateia & Nowell, 2004).

Espie's model provides a slight variation from Spielman's model, but is complementary to the underlying theoretical underpinnings of the links between sleep and arousal. The unique contributing factor is the explanation of how the normal night-to-

night variations of sleep become chronic problems for some sleepers. However, the model does not fully describe how other biological problems (e.g., pain) impact sleep. As with Spielman and Harvey, Espie focuses solely on the concepts related to insomnia limiting its use in other sleep-wake disturbances.

In summary, there are a variety of theoretical models that attempt to conceptualize the problem of sleep-wake disturbances. Although the models provide important links between physiological and psychological factors, they are generally unsupported by research and lack generalizability to various population. Without accurate conceptualization through empirically tested theoretical models, it is difficult to develop effective individualized interventions and ascertain what types of interventions may be effective for a specific problem or population.

Interventions for sleep-wake disturbances

Interventions for sleep-wake disturbances include both pharmacologic and non-pharmacologic treatments. Although not the focus of this study, intervention remains an important topic to review in order to build the case for the study of predictors of sleep-wake disturbances. In order to effectively treat sleep-wake disturbances it is essential to evaluate the underlying factor(s), or predictors, causing the disturbance. Therefore, this section will provide a brief overview of the pharmacologic and non-pharmacologic treatments used for sleep-wake disturbances.

Pharmacologic interventions

Pharmacologic agents have been refined as scientists discovered the relationship between neurotransmitter action and sleep. The study of neurotransmitter activity prompted the development of drug classifications called benzodiazepines and non-

benzodiazepines. Benzodiazepines are the traditional agents used for short-term treatment of sleep-wake disturbances (Holbrook, Crowther, Lotter, Cheng, & King, 2000b; Mendelson et al., 2004; Wagner, Wagner, & Hening, 1998). Benzodiazepine compounds are agonists that mimic the action of the neurotransmitter GABA. Non-benzodiazepines are considered the new generation of sedative-hypnotics (Mendelson et al., 2004; Terzano, Rossi, Palomba, Smerieri, & Parrino, 2003; Wagner et al., 1998). The mechanism of action for non-benzodiazepines is similar to benzodiazepines but binding is selective to certain receptor sites, thus are more selective in their action. The increased selectivity has reduced the side effect profiles and the drug treatment of choice for sleep-disturbances (Wagner et al., 1998). Both types of drugs remain the most prescribed hypnotics for the treatment of sleep-wake disturbances (Benca, 2005).

Non-pharmacological interventions

Non-pharmacological treatments, known as cognitive-behavioral therapy (CBT), attempts to identify, challenge, and alter dysfunctional beliefs and attitudes about sleep (Quesnel, Savard, Simard, Ivers, & Morin, 2003). Types of CBT include behavioral (e.g., stimulus control, sleep restriction, exercise), cognitive (e.g., cognitive restructuring), and educational (e.g., sleep hygiene, stress management) (Morin et al., 1999; Savard et al., 2005a; Savard, Simard, Ivers, & Morin, 2005b). Although efficacy has been established through controlled trials, these interventions are time intensive, require a trained sleep specialist for delivery, and are limited to specific types of sleep-wake disturbances (e.g., poor sleep hygiene, insomniacs) (Petit, Azad, Byszewski, Sarazan, & Power, 2003; Quesnel et al., 2003; Savard et al., 2005a).

The following section reviews sleep in BCS. This extensive overview was intended to show the complexity of sleep physiology, how sleep is operationally defined, pertinent classifications for clinical diagnosis, negative consequences associated with sleep-wake disturbances, and common interventions used to promote better sleep in BCS. Knowledge gained from this section shows multiple areas for potential physiological etiologies in BCS with disturbed sleep.

Part II: Sleep in BCS

Part II of this chapter links the overview of sleep with sleep-wake disturbances that occur during breast cancer survivorship. In order to better understand why this is an important problem in this population the following section focuses on; (a) methodological issues of sleep-wake research in BCS, (b) theoretical issues of sleep-wake research in BCS, (c) predictors of sleep-wake disturbances in BCS, and (d) sleep interventions studied in BCS.

Searches were conducted to find descriptive and intervention research related to sleep-wake disturbances in breast cancer. Using MEDLINE®, CINAHL®, PubMed, and the American Psychological Association's Psych INFO, 515 articles were found using sleep and cancer, sleep-wake and cancer, and sleep-wake and breast cancer survivor, treatment, intervention as search terms. Of these articles, 35 addressed sleep as a primary or secondary outcome and 5 addressed interventions specifically for sleep-wake disturbances in BCS (see APPENDIX B). Articles were a mix of descriptive findings, pertinent reviews, and experimental designs. One note of interest, the most recent descriptive article specific to BCS was last published in 2004 showing the limited nature of current findings.

Methodological issues of sleep-wake research in BCS

The following section addresses the current methodological issues of sleep-wake research in BCS. The section covers seven main topics; (a) prevalence; (b) comparative studies; (c) sleep studies over-time; (d) sleep as a primary variable; (e) measurement of sleep; (f) sleep terminology and diagnosis in BCS research; and (g) consequences of sleep-wake disturbances in BCS.

Prevalence

Beast cancer survivors (BCS) represent the largest proportion of cancer survivors. It is estimated that 22% or 2.2 million of the 9.8 million cancer survivors in the United States are BCS (National Center for Chronic Disease Prevention and Health Promotion, 2004). This number is projected to increase each year (Jemal et al., 2008). Current evidence suggests that a significant proportion of BCS suffer from poor sleep quality. Researchers have found that 19-90% of BCS complained of poor sleep or insomnia (Carpenter & Andrykowski, 1999; Carpenter et al., 2004; Crandall et al., 2004; Davidson et al., 2002; Fortner et al., 2002; Northouse et al., 1999; Savard, Simard, Blanchet, Ivers, & Morin, 2001; Schultz, Klein, Beck, Stava, & Sellin, 2005) which can last several years after the original diagnosis (Berger et al., 2005; Carpenter et al., 2004; Elam & Carpenter, 2004b; Savard et al., 2001). The prevalence of sleep problems in BCS is stated to be higher than the general population (20% in both male and female) and other cancer types (e.g., 32% in gastrointestinal) (Davidson et al., 2002; Savard et al., 2001). Although studies consistently report that sleep is a problem in BCS, findings are plagued with inconsistent theoretical models, terminology, and measures of sleep.

The accuracy of prevalence statistics of sleep-wake disturbances in BCS is unclear due to several methodological issues. Issues included lack of comparative studies (BCS vs. non-cancer women), inconsistent diagnostic terminology (DSM-IV vs. ICSD-9 vs. generic terminology), lack of consistent measurement of sleep (objective vs. subjective), lack of longitudinal studies, and lack of ethnically diverse samples. In addition, current studies focus on subgroups of women (e.g., metastatic breast patients, newly diagnosed) leaving gaps in the survivorship literature (Berger & Higginbotham, 2000; Fortner et al., 2002; Koopman et al., 2002). In the following section the methodological limitations are discussed in detail.

Comparative studies

It is unclear whether the prevalence, severity, or predictors of sleep-wake disturbances differ between BCS and age-matched WWBC. It seems logical to compare BCS with WWBC since survivors tend to re-enter regular health practices after treatment is completed. The salient difference between BCS and WWBC is the experience and treatment of cancer. Although findings show as many as 23-51% of healthy women report sleep-wake disturbances, few studies directly compare the two populations (Fortner et al., 2002; Kravitz et al., 2003; Shaver & Zenk, 2000). In one comparative study of BCS (n=15) and healthy women (n=15), a majority of participants in both groups had poor sleep quality and high sleep disturbance (73% of BCS and 67% of healthy women above a cutoff score of 5) (Carpenter et al., 2004).

In terms of predictors, some BCS experience poorer sleep quality and higher sleep disturbance in comparison to their age-matched counterparts without cancer due to intense menopausal symptoms related to hormonal therapy, (Carpenter & Andrykowski,

1999; Mourits et al., 2002; Savard, Davidson et al., 2004), residual side effects from cancer treatment (Hunter et al., 2004), increased circadian rhythm disruptions due to cancer-related treatment (Carpenter, Gautam, Freedman, & Andrykowski, 2001; Roscoe et al., 2002), more intrusive thoughts (Bleiker et al., 2000), greater psychological distress related to diagnosis and treatment (Savard et al., 2001), poorer sleep hygiene behaviors (Berger et al., 2003), and/or more intrusive sleep environments (Davidson et al., 2002). Sleep duration was significantly shorter for BCS (n=15) compared to WWBC (n=15) ($p<0.05$), but for both survivors and controls, global sleep scores were significantly, positively correlated with fatigue and depression (Carpenter et al., 2004). Predictors of sleep-wake problems in either population were not evaluated in this study. Similarly, a comparative study of disease-free BCS (n=150) and WWBC (n=78), researchers found that sleep problems and depressive symptoms are significantly higher among highly fatigued BCS compared to those who are not as fatigued (Servaes, Verhagen, & Bleijenberg, 2002). Based on these results, BCS seem to have greater sleep disturbance, more depressive symptoms, and greater levels of fatigue compared to WWBC.

Sleep over time in BCS

There have been few large, longitudinal comparative studies focusing on sleep in breast cancer (Davidson et al., 2002). The majority of research focuses on breast cancer patients undergoing adjuvant high-dose treatment or treatment for metastatic disease and rarely follow subjects over time (Berger & Farr, 1999; Berger et al., 2002; Berger et al., 2003; Fortner et al., 2002; Kopelman, Apps, Cope, & Empey, 1985). During treatment, more daytime and less nighttime sleeping are related to higher on-treatment fatigue (Berger & Farr, 1999; Roscoe et al., 2002) and higher depressive symptoms (Roscoe).

Although Berger reassessed sleep one year after cancer treatment, the results did not address potential sources of the continued sleep problems (Berger et al., 2002; Berger et al., 2003). Other studies focusing on BCS, those with metastatic disease, or those with other co-morbidities were not cross-sectional and did not evaluate whether sleep problems existed before treatment and/or when they developed during treatment (Davidson et al., 2002; Deimling et al., 2002; Fortner et al., 2002; Servaes, Verhagen et al., 2002). Therefore, we do not know whether or how sleep problems may change over the course of the cancer trajectory.

Researchers suggest sleep changes initially encountered during cancer treatment may become chronic (Ancoli-Israel et al., 2005; Savard, Davidson et al., 2004; Savard et al., 2001) and that the respective relationships between sleep and fatigue and sleep and depressive symptoms continue post-treatment and into the period of cancer survivorship. Despite using different measures for sleep, findings across studies of BCS indicate that chronic poor sleep quality does occur and is correlated moderately with post-treatment fatigue ($r=|0.38\text{-}0.68|$, $p<0.05$) (Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998; Carpenter & Andrykowski, 1998; Okuyama et al., 2000) and with post-treatment depressive symptoms ($r=0.50\text{-}0.63$, $p<0.001$) (Carpenter & Andrykowski, 1998; Okuyama et al., 2000).

Sleep as a primary variable

The existing literature focuses on sleep problems in BCS as a secondary variable or outcome of another research variable (e.g., fatigue). Of the descriptive articles reviewed, 13 focused on fatigue and other quality of life issues listing sleep as an outcome. Literature suggests that sleep-wake disturbances frequently emerge as a

significant problem in studies primarily examining fatigue, depression, decreased quality of life, and/or menopausal symptoms (Ancoli-Israel et al., 2001; Bleiker et al., 2000; Northouse et al., 1999). This limits our understanding of sleep and cancer to certain symptomatic conditions (e.g., chronically fatigued BCS) (Savard & Morin, 2001; Savard et al., 2001). Whether sleep was the primary complaint in these women is unclear limiting knowledge regarding the etiology and timing of sleep problems in BCS.

Measurement of sleep in BCS

Part of the struggle in the BCS literature is lack of sonsistent measures to evaluate sleep. Eight of the reviewed studies used the Pittsburgh Sleep Quality Index (PSQI) (Andrykowski, Curran, & Lightner, 1998; Berger et al., 2003; Broeckel et al., 1998; Carpenter & Andrykowski, 1998; Carpenter et al., 2004; Fortner et al., 2002; Spelten et al., 2003; Weitzner, Moncello, Jacobsen, & Minton, 2002), 5 studies used actigraphy (Berger & Higginbotham, 2000; Berger et al., 2002; Berger et al., 2003; Miaskowski & Lee, 1999; Roscoe et al., 2002), and only one used PSG (Roscoe et al., 2002) to measure sleep (see APPENDIX B). Because sleep was not the primary outcome for most of the reviewed studies, this lack of consistent measures limits overall knowledge and contributes to the variability in prevalence rates. In addition, since there are validated measures for use in cancer populations, it remains unclear why there is such inconsistent use of measurements of sleep. Recommendations have been made for the standardization of sleep measurement in order to facilitate meta-analyses within the descriptive work in cancer populations (Clark et al., 2004; Vena et al., 2004).

Terminology and diagnosis in BCS

There is a lack of consistent terminology used to describe sleep-wake disturbances in BCS. In addition, there are no current studies that evaluate how practitioners assess sleep problems in the cancer population (Berger et al., 2005; Clark et al., 2004). This can be attributed to several research issues.

First, research studies typically use generic terms that are intermixed with clinical terminology (e.g., sleep latency and insomnia). Although descriptive findings provide valuable information regarding sleep-wake disturbances in BCS, inconsistencies in terminology make translation of findings into guidelines for clinical practice difficult. For example, Savard et al. (2005) studied the prevalence of insomnia using DSM-IV criteria in breast cancer patients (n=145) and found 61% experienced high sleep latency (longer than 30 minutes to fall asleep) and frequent nighttime awakenings (73%) lasting several months after diagnosis of cancer (M=60 months). In addition, Davidson et al. (2002) used a sleep survey with general sleep questions and reported women with breast cancer (n=302, in-treatment and survivors) experienced symptoms of restless leg syndrome (42.7%, range=37-49%), insomnia (37.8%, range=32-44%), and interruptions in breathing during sleep (9.6%, range=6.5-14%). Conversely, Carpenter et al. (2004) used general terms from PSQI results (e.g., sleep quality, global sleep scores) and found 73% of BCS experienced poor sleep quality (above cutoff of 5 for poor sleep quality), high sleep disturbance, and short sleep duration (<6 hours per night). For the clinician, these inconsistencies provide little information about the true prevalence and etiology of the problem. Without clear prevalence and etiology, it is difficult to formulate clinical practice guidelines for evaluation and treatment of sleep problems in cancer patients.

Thus, there is currently no established evidence based guidelines for the diagnosis of sleep-wake disorders in the cancer population.

Second, ICDS-R and DSM-IV criteria are typically used by trained sleep specialists and/or psychologists and are rarely used in general practice (e.g., oncology or general medicine) (Berger et al., 2005). Oncology practitioners and clinicians rarely have the time or expertise to perform the intensive sleep assessment required to diagnose ICDS-R or DSM-IV disorders. Thus, there is a need for consistent diagnostic criteria (generic or ICDS-R) to help provide conceptual clarity in order to formulate future diagnostic guidelines for specific populations such as cancer. There is current support for the use of ICDS-R since it originates from the American Academy of Sleep Medicine (Berger et al. 2005). However, clinicians outside of the discipline of sleep medicine need additional training in order to use these categories appropriately. Ultimately, better diagnostic practices will contribute to better interventions for this problem.

Immediate and delayed consequences

It is difficult to ascertain the negative effects of sleep-wake disturbances specific to BCS. Because studies do not consistently use sleep as a primary outcome, similar measurements, or similar terminology, the immediate and delayed outcomes for BCS are unclear. In addition, studies often report the characteristics of sleep disturbances but fail to assess potential negative consequences (Davidson et al., 2002; Fortner et al., 2002; Savard et al., 2001).

In studies where consequences were reported, findings suggest that fatigue, impaired daytime functioning, mood disturbance, social dysfunction, and altered cognitive function result from poor sleep (Anderson et al., 2003; Carpenter et al., 2004;

Savard, Laroche, Simard, Ivers, & Morin, 2003; Savard & Morin, 2001). One study linked consequences to quality of life scores using a standardized quality of life questionnaire (SF-36) and found higher sleep disturbance scores resulted in significant deficits in health related quality of life (n=72) (Fortner et al., 2002).

Because studies do not report sleep-wake disturbances over-time, the chronicity of negative consequences is also unclear. Future studies are needed to determine specific consequences to BCS.

Theoretical aspects of sleep-wake research in BCS

Although there are theoretical models (e.g., Two Process Model) that provide valuable sources of information regarding concepts of sleep, the BCS literature has failed to produce an overarching model that encompasses predictors and outcomes of sleep-wake disturbances. Therefore, the purpose of this last section is to describe the; (a) current theories used in the BCS literature and (b) support for the list of predictors selected for inclusion in the Elam Psychobiological Model.

Current theories in BCS literature

Of the descriptive BCS studies reviewed with sleep as the primary outcome, only 5 articles used theoretical models to guide their research (see APPENDIX B) (Berger et al., 2003; Carpenter et al., 2004; Savard et al., 2001). Of these models, only two were specific to sleep (Spielman's Psychobiological Model and Borbely's Two-Process Model) (Clark et al., 2004; Savard et al., 2001; Vena et al., 2004). As noted in the above review, these two models are limited to either physiological and/or psychological factors that contribute to sleep-wake disturbances. Although there are known factors that contribute to sleep disruptions in BCS (e.g., being female, increased age, depression, general

anxiety), current models do not adequately explain how physiological (e.g., pain, cancer treatment side effects), psychological (e.g., cancer distress), environmental (e.g., bedroom temperature), and pre-sleep routines (e.g., sleep hygiene habits) co-contribute to the occurrence of sleep-wake disturbances and resulting negative consequences.

Because BCS experience multiple predictors (physiological, psychological, environmental, sleep-hygiene) that contribute to possible sleep problems, a new model was developed to link predictors of sleep-wake disturbances in BCS with the negative consequences.

Predictors in Elam model

Since the majority of sleep disturbance studies in the BCS have not evaluated a comprehensive set of predictors, the following is a discussion of possible physiological, psychological, environmental, and sleep hygiene factors that can negatively impact sleep in BCS. This review provides rationale for inclusion in the BCS sleep-wake disturbances model. Although included in the exploratory model, not all predictors listed will be evaluated for this study (see Chapter Three for list of predictors to be evaluated for this study).

Person characteristics as predictors.

Person characteristics such as age, race, socioeconomic status, education, and menopausal status are known predictors of sleep-wake disturbances. Since these factors are known predictors of sleep-wake disturbances, they are typically controlled for in statistical analyses (Vena et al., 2004). However, it is important when comparing BCS and WWBC that these be evaluated as predictors if the populations are uniquely different in demographic and other characteristics.

Physiological predictors.

Physical factors that predict sleep-wake disturbances in BCS are co-morbid conditions (e.g., thyroid dysfunction, immune dysfunction) (Espie, 2002; Harvey, 2002; Holbrook, Crowther, Lotter, Cheng, & King, 2000a), menopausal symptoms (e.g., hot flashes, urinary frequency) (Carpenter & Andrykowski, 1999; Couzi, Helzlsouer, & Fetting, 1995; Fortner et al., 2002; Savard, Davidson et al., 2004; Shaver & Zenk, 2000), and/or long-term side effects that linger after cancer treatment (e.g., pain). There are a limited number of studies focusing on the physiological predictors of sleep in cancer patients. Prior studies have not consistently examined use of medications that may affect sleep (e.g., antiemetics, pain medications, antidepressants). In addition, it is not clear whether or how the long-term effects of cancer treatments affect essential neuroendocrine and/or other physiological processes (e.g., circadian function) involved in sleep (Berger & Farr, 1999; Berger et al., 2002; Davidson et al., 2002; Engstrom et al., 1999; Roscoe et al., 2002).

Co-morbid conditions.

There are a number of co-morbid conditions that negatively impact sleep but, generally these are not linked to the occurrence of sleep-wake disturbances in BCS. Thyroid and immune dysfunction are two areas that have provided some information regarding this link. Those not addressed below such as diabetes, high blood pressure, osteoarthritis, or lung disease were not found in the BCS literature but warrant further investigation.

Thyroid function. There is growing evidence that BCS experience thyroid dysfunction after cancer treatment (Anker, Lonning, Aakvaag, & Lien, 1998). Women in

general have high prevalence rates of thyroid dysfunction that typically present during peri-and post menopause. According to the American Association of Clinical Endocrinologists, 1 in 8 women between the ages of 35 and 65, and, 1 in 5 over the age of 65 experience thyroid dysfunction (http://www.aace.com/, 2006).

Unfortunately, symptoms of menopause experienced by BCS mimic thyroid dysfunction, thus, a significant proportion of women are undiagnosed (Anker et al., 1998). BCS are reported to be more prone to thyroid dysfunction due to cancer treatment, premature ovarian failure, and use of estrogen modulators (Anker et al., 1998). The link among these factors remains unclear. A current study compared breast cancer patients with healthy controls and found 46% (n=102) had thyroid disease after the treatment of breast cancer (Giani et al., 1996). Because abnormal thyroid function can be both the underlying etiology (e.g., thyroid enlargement) and a consequence of hormonal changes/metabolism, clinical evaluation of thyroid function should be performed in women complaining of sleep problems. In the BCS, no current studies performed serum tests of thyroid function prior when assessing sleep.

Post-menopausal symptoms. Estrogen is purposely ablated in women with hormone receptor positive cancers. Medications are taken to shut down the estrogen supply to certain areas of the body to prevent cancer recurrence. This sudden decrease in estrogen can contribute to menopausal symptoms such as hot flashes and low/poor bone density.

Women who experience hot flashes tend to report poor sleep quality on subjective measures (Carpenter et al., 2002). Descriptive studies show that BCS have more frequent and more severe hot flashes than healthy women (Carpenter et al., 2002). It has been

reported that 48% of BCS report hot flashes that contribute to nighttime restlessness and awakenings interfering with sleep (Carpenter, 2000; Carpenter et al., 2001). Savard et al. (2004) found significant relationships between nighttime hot flashes and sleep (n=24 BCS). Findings suggested that nighttime hot flashes contributed to less efficient and more disrupted sleep (F=4.98, p=0.038). Fortner et al. (2002) found that 61% of a breast cancer sample showed global sleep scores greater than the established cut-off for disturbed sleep (n=72). Carpenter & Andrykowski (1999) examined physical menopausal symptoms in 114 BCS. Trouble sleeping was reported by 68% of these women.

Other menopausal symptoms such as urogential changes (e.g., vaginal dryness, urinary frequency), increased weight gain, and altered body image have not been linked to sleep-wake disturbances. One study reported that 50% of the breast cancer patients indicated they woke at least 3 times per week to use the bathroom (Fortner et al., 2002). Because a majority of BCS are estrogen deprived, these symptoms could be possible predictors of sleep disturbances in this population.

Long-term cancer related side-effects. The literature reveals some insight into the physiological side effects of cancer treatment and sleep disturbances. Cancer patients experience side effects related to the disease itself such as pain and altered activity (Vena et al., 2004). It has been well established that sleep is disrupted by pain (Cleeland, 1993; Vena et al., 2004). Studies show that up to 80% of cancer patients experience pain during and after cancer (Higginson & Hearn, 1997; Vena et al., 2004). Pain can become chronic due to multiple breast surgeries and reconstruction resulting in chronic muscular pain. Increased sleep in cancer patients was found to decrease pain. One study found that the administration of sleep-inducing protein (tryptophan) increased deep sleep and reduced

pain (Donovan & Dillon, 1987). Pain can also be related to chemotherapy and radiotherapy. Although these side effects typically subside over time, chronic pain has been noted in some long-term BCS (Clark et al., 1995).

Women with metastatic disease are known to have increased bone pain resulting in poor sleep (Cleeland et al., 1994; Dow et al., 1996). However, because women without metastatic disease experience frequent nighttime awakenings, it is unclear if chronic pain is a factor. Therefore, further investigation is needed to clarify the links between pain and sleep disorders in BCS.

The use of supportive care medications during cancer treatment is essential to reduce unwanted side effects of the treatment (e.g., nausea, vomiting). Such agents as steroids used for nausea have been linked to sleep-wake disturbances during and after cancer treatment (see APPENDIX D) but often resolve after the drug is stopped. The continued use of specific supportive care medications (e.g., anti-anxiety and opioids) has not been studied in longitudinal research looking at the negative effects of these supportive care medications over-time.

Physical activity. The role of physical activity has received some attention in the breast cancer literature. The majority of this research focuses on activity level in relation to fatigue outcomes for women undergoing active treatment for breast cancer. Studies show that activity level decreases during chemotherapy or radiation therapy prompting high levels of fatigue (Berger, 1998; Graydon, Bubela, Irvine, & Vincent, 1995; Mock et al., 2001). This decrease in activity and high level of fatigue have been related to sleep-wake disturbances (Berger, 1998; Berger & Farr, 1999). Interventions focus on education of sleep hygiene practices (pre-sleep routines) and exercise regimens that increase

activity (Berger, 1998; Berger & Farr, 1999; Mock et al., 1997; Mock et al., 2001). This increased activity has lead to decreases in sleep-wake disturbances and fatigue levels in patients undergoing active treatment. However, it is unclear if the decrease in activity experienced during treatment continues into survivorship. It is also unclear if the ability to perform certain physical activities, or level of physical functioning (e.g., ability to walk up a flight of stairs), has an impact sleep. Therefore, it is important to include physical activity or function in the model to determine if it is related to occurrence of sleep-wake disturbances.

Genetics. The link between genetic polymorphisms and sleep-wake disturbances in BCS has been investigated. Although genetic variations are not included in the Elam theoretical model, links between circadian genes and breast cancer is receiving more attention in the literature. It has been reported that the growth of cancer has been linked to the circadian gene expression (Chen et al., 2005; Eriguchi et al., 2003; Filipski et al., 2002; Mormont & Levi, 2003; Stevens, 2005; You et al., 2005). Tumor cells are rhythmically expressed each day within the peripheral tissue but are destroyed by natural defense mechanisms. Chen et al. (2005) found specific gene variants to be a risk factor for breast cancer in a group of Taiwanese women. The study showed that 95% of breast tumors revealed abnormal circadian gene expression compared to non-cancerous cells near the tumor (Chen et al., 2005). It remains unclear if abnormal circadian gene expression are the reason for the erratic circadian patterns of cortisol and melatonin secretion found in BCS (Rich et al., 2005; Sephton et al., 2000). This is one area of research that shows great promise in identifying possible genetic links of sleep-wake disturbances in BCS.

Psychological predictors.

Psychological precipitating and perpetuating factors include cancer related distress (concerns of recurrence) and general psychological distress (anxiety and depression). Although these issues are found in non-cancer populations, BCS are unique in that they live with the constant concerns of cancer recurrence (Turner, Kelly, Swanson, Allison, & Wetzig, 2005). In addition, menopausal symptoms are also linked to the development of depression, anxiety, and general distress making it difficult to differentiate these symptoms from similar cancer related depression, anxiety, and distress (Dzaja et al., 2005; Jones & Czajkowski, 2000; Sharkey et al., 2003; Shaver & Zenk, 2000).

The majority of studies that focus on psychological factors target populations that are newly diagnosed, undergoing treatment, and/or at the end of life (Berger & Higginbotham, 2000; Davidson et al., 2002; Savard et al., 2001). In addition, articles reviewed tend to report sleep disturbances as a consequence of life stressors (e.g., low social support, work, bereavement) not as a predictor (Berger & Walker, 2001; Clark et al., 1995; Davidson et al., 2002; Fortner et al., 2002; Koopman et al., 2002; Savard et al., 2001). Redeker et al. (2000) found that fatigue, depression, and anxiety during chemotherapy treatment predicted insomnia ($r=0.26-0.69$, $p<0.001$). In addition, Koopman et al. (2002) examined sleep patterns in women with metastatic breast cancer and found women with more bone lesions had higher levels of pain and depression reflecting the overlapping nature of predictors. Carpenter et al. (2004) looked at sleep, fatigue, and depressive symptoms in BCS with hot flashes and found fatigue and depressive symptoms were related to poor sleep quality ($r=0.43-0.47$, $p<0.005$). These

studies are limited by the population studied (women with hot flashes or metastatic disease) and exclusion of other potential predictors of sleep disturbances (e.g., environmental factors).

Environmental and sleep hygiene predictors.

Environmental factors have not been fully evaluated in the breast cancer literature. Environmental factors include sleep environment, companion sleep, and care of dependents in the home (e.g., elderly parents, children). It is known that lingering effects of cancer treatment can disrupt environmental cues for sleep (Lavie, 2001). Side effects such as nausea, vomiting, diarrhea, and general malaise are most severe during treatment and subside 1-2 weeks post treatment. Because of these side effects, normal environmental cues can be disrupted by frequent napping, nighttime awakenings, and decreased physical activity (Berger & Farr, 1999; Mock et al., 1997). If environmental cues are disrupted, the circadian cycle generally becomes out of sync causing shortened sleep cycles (Borbely & Achermann, 1992) leading to daytime sleepiness because the amount of restorative sleep was not adequate.

Sleep hygiene factors (e.g., pre-sleep routines) can also contribute to sleep-wake disturbances (Berger et al., 2002). Within the BCS literature, studies did not evaluate whether sleep problems existed before treatment and/or when they developed during treatment (Davidson et al., 2002; Deimling et al., 2002; Fortner et al., 2002; Savard et al., 2001). Although sleep hygiene factors were evaluated as part of Berger's (2003) intervention for sleep and fatigue, the intervention did not assess other possible predictors of sleep disturbances. In addition, Berger did not report specific factors that emerged from the sleep hygiene assessment prior to intervention. These limitations provide little

information regarding how sleep hygiene affects sleep in BCS. However, sleep hygiene factors are shaded in gray and will not be evaluated in this study due to measurement constraints (see Chapter Five).

Based on this discussion, it is noted that a complete set of predictors for sleep-wake disturbances are rarely evaluated in the BCS literature. There are several areas of potential interaction among predictive factors and the occurrence of sleep disturbances. It is important to examine these predictive factors in order to determine effective interventions that prompt sleep in this population.

Interventions studied in BCS

It remains unclear what types of treatments are commonly used by BCS (outside of research) and are effective for sleep-wake disturbance. The following is a review of the types of sleep interventions that have been studied in BCS.

Pharmacological studies in BCS

Women with breast cancer have been noted to use hypnotics to facilitate sleep. Recent studies show, 20%-40% of BCS report using pharmacologic agents to promote sleep (Davidson et al., 2002; Savard et al., 2005a). This range is comparable to other cancer populations except for lung cancer where over 40% report use of these agents (Davidson et al., 2002). No controlled studies were found that examined the efficacy of these agents in BCS. Although studies show these agents are commonly used, BCS's desire to take additional medications is low (Vena et al., 2004). This lack of interest is reflected in a comment made by a survivor participating in a behavioral hot flash research study (Carpenter et al., 2007).

> "…..we (BCS) don't want to take medication (for sleep-wake disturbances)…We feel like we are dumping enough chemicals into our bodies."

This statement provides only one viewpoint but reflects possible barriers to performing controlled drug trials in this population.

Non-pharmacologic interventions in BCS

The review of non-pharmacologic intervention studies produced five articles that were specific to BCS (Berger et al., 2003; Davidson, Waisberg, Brundage, & MacLean, 2001; Quesnel et al., 2003; Savard et al., 2005a; Shapiro, Bootzin, Figueredo, Lopez, & Schwartz, 2003). Results were mixed regarding the benefit of non-pharmacological interventions for BCS (Berger et al., 2003; Davidson et al., 2001; Quesnel et al., 2003; Savard et al., 2005a; Shapiro et al., 2003). First, Berger et al. (2003) conducted a prospective, sleep promotion intervention study with 21 BCS. Women were assessed at 30, 60, and 90 days after completion of cancer treatment. Results showed high adherence rates to a sleep promotion intervention (77%-88%) supporting the feasibility of the intervention. Although no changes in fatigue were noted over time, the intervention decreased sleep latency (less than 30 minutes) and nighttime awakenings (10-11 times/night), increased sleep efficiency (82-92%) and total sleep time (7-8 hrs) (Berger et al, 2003).

Davidson et al. (2001) found improvements in sleep, mood, and daily functioning using a group sleep therapy intervention. The quasi-experimental study examined the efficacy of a sleep therapy program in 15 cancer survivors (some with metastatic disease) with insomnia. The sample was a non-depressed, non-anxious group with adequate scores on the quality of life measures. Sleep outcomes showed significant

decreases in number of nighttime awakenings (F=8.63; p=0.002), wake after sleep onset (F=15.61; p=0.001), and sleep impairment ratings (F=29.19; p<0.001) after the 8-week intervention. Increases in total sleep time (F=4.12; p=0.030), percent sleep efficiency (F=31.29; p<0.001), and feelings of being rested (F=9.50; p=0.003) were also found.

Quesnel et al. (2003) found similar results in terms of sleep and mood using sleep therapy intervention in a single group of non-metastatic BCS (n=10). Subjects participated in group sessions that provided education regarding good sleep hygiene practices. Sleep variables improved over time with the use of the group therapy intervention. Reductions in wake after sleep onset (s=-15, p=0.02) and increases in sleep efficiency (s=13, p=0.04) were found comparing pre-treatment to post-treatment and post-treatment to 6 month follow-ups. Depression scores, although non-significant, decreased from a baseline mean of 10.8 on the Beck Depression Inventory to a mean of 5.3. Likewise, anxiety, fatigue, and quality of life improved and although not statistically significant, provided support for clinical significance of the intervention for the improvement of sleep and mood.

Savard et al. (2005a) conducted a randomized-controlled trial of 57 BCS with insomnia that was attributed to the diagnosis or treatment of breast cancer. Women were randomized to cognitive-behavioral treatment (n=27) or the wait-list control (n=30). Results showed significant (p<0.001) group-time interaction for variables except total sleep time. Sleep efficiency (F=22.59), total wake time (F=22.77), sleep onset latency (F=4.16), and wake after sleep onset (F=16.7) were significantly different between groups. Sleep measured by PSG found no significant group-time interactions with any sleep variables supporting the disconnect between perceived self-reported sleep and

results of objective findings. Quality of life scores did improve reflected by significant ($p<0.05$) group-time interactions on scores of anxiety ($F=5.19$), depression ($F=4.14$), and global quality of life ($F=5.69$). Together, the improvement of sleep and quality of life were valuable but were not sustained over-time.

Finally, Shapiro et al. (2003) conducted a sub-study of the efficacy of a mindfulness-based stress intervention for sleep disturbances in non-metastatic BCS ($n=63$). The intervention consisted of 6-weekly sessions using three types of meditation. Subjects could self-select into a control group that included only self monitoring practices using written materials from the study staff. Results were not generally favorable for the reduction in sleep-wake disturbances. Baseline assessments revealed participants had mild to moderate degrees of sleep complaints. Those participants with greater levels of distress at baseline had significantly lower sleep quality and general feelings of being refreshed after sleep throughout the entire intervention and follow-up regardless of group assignment. When distress was controlled for in the data analysis, sleep efficiency was not significantly improved with the intervention.

Limitations

Although pharmacological interventions have not been formally tested in BCS, research suggests that non-pharmacological interventions in BCS can be beneficial but these improvements in sleep often are not sustained over-time. Problems with non-pharmacological interventions were attributed to the time-intensive nature of the interventions due to number of therapy sessions needed with a trained sleep specialist. In addition, due to high participant withdrawal, adherence over time was not been well-

established, thus, the long-term benefits are unknown (Berger et al., 2002; Davidson et al., 2001; Quesnel et al., 2003; Savard et al., 2005a; Shapiro et al., 2003).

In sum, sleep-wake disturbances are a common problem reported by BCS. Because sleep is such a vital function, disruptions in sleep can lead to a multitude of negative consequences. Unfortunately, sleep disturbances in BCS are often not assessed in clinical practice and often go untreated due to complex diagnostic criteria and lack of clinical guidelines for non-sleep specialty clinicians (Vena et al., 2004). The use of evidence-based guidelines is limited due to the problems with the current literature. Limitations in the descriptive and intervention studies decrease our understanding of conceptual links between sleep and sleep disturbances.

Based on this extensive review of BCS literature, the following research questions emerged this study.

1. Is there a difference in the prevalence of sleep-wake disturbances between BCS and WWBC?
2. Is there a difference in severity of sleep-wake disturbances between BCS and WWBC?
3. Is there a difference in the physiological, psychological, and environmental predictors of poor sleep in BCS and WWBC?
4. Is there a difference in the physiological, psychological and environmental predictors of the severity of sleep-wake disturbances between BCS and WWBC?

Answering these questions will improve conceptual clarity through knowledge of predictors of sleep problems which will help target effective treatments and improve quality of life in this unique population.

CHAPTER THREE

METHODOLOGY

The purpose of this chapter is to describe the proposed methodology for this study evaluating predictors of sleep-wake disturbances in BCS compared to age-matched WWBC. The chapter is organized into two parts; (1) methods of the parent studies that provided data for this study and (2) methods of this study of sleep-wake predictors.

Part 1: Parent Studies

The parent dataset consisted of data being collected from two studies; the American Cancer Society Quality of Life Study (ACS) (#RSGPB-04-089-01-PBP, Champion PI) and the Survey of Quality of Life in African American Women (AA) (NCI #R03 CA-097737 & Walther Cancer Institute, Russell PI). The first part of this chapter will describe four aspects of the parent studies; (1) design, (2) sample criteria, (3) recruitment, and (4) data collection. Because both parent studies are similar, descriptions were combined within each sub-section with differences noted when applicable.

Design

Both parent studies were cross-sectional, descriptive, comparative, case-controlled designs evaluating an extensive set of quality of life variables in BCS. Data were collected via questionnaire survey at a single point in time.

Sample criteria

The parent studies had similar inclusion and exclusion criterion. The overall goal of both studies was to compare quality of life in BCS and age-matched WWBC. The following is a list of inclusion criterion for BCS and WWBC for both studies.

BCS

1. Provided informed consent.
2. Able to read, write, and speak English.
3. In good general health.
4. First-time diagnosis of breast cancer.
5. No other known cancer at the time of the study.
6. Cancer-free at time of study enrollment (stage I-III).
7. At least two years (Russell study) or three years (ACS study) post-completion of surgery, radiation, and chemotherapy. No more than 8 years post-diagnosis for the ACS study.
8. Must be between 18 and 45 years of age or between 55 and 70 years of age at diagnosis for the ACS study and over age 18 for the Russell study.

WWBC

1. Provided informed consent.
2. Age 18 years or older.
3. Able to read, write, and speak English.
4. In good general health.
5. No known cancer at the time of the study.
6. Matched to a BCS on age (+/- 5 years) and education (similar education).

Recruitment

Both parent studies used similar local recruitment strategies while the ACS also recruited women outside of the local area. BCS and WWBC participants for the ACS and AA study were recruited using the following strategies; (a) telephone and local clinic

contacts, (b) referrals from other institutions outside of Indiana (ACS only), and (c) acquaintance control referrals.

Telephone and local clinic contacts

Telephone and local clinic contacts were performed as follows. BCS were recruited from the Indiana University Simon Cancer Center (IUSCC) and Wishard Memorial Hospital. These clinics were chosen based on availability of participants for this geographic location. Telephone contacts occurred as follows. Women referred by recruiters or physicians were screened via the telephone by a trained study team member for eligibility and informed of the purpose and nature of the parent study. Study team members completed and passed the "Human Subjects Certification Test" at Indiana University School of Nursing (IUSON) prior to participant contact. Eligible women were mailed two copies of the consent and Health Insurance Portability and Accountability Act (HIPAA) authorization form and a stamped, self-addressed envelope for returning their signed consent.

Women recruited in-person during clinic hours were approached by a designated study member after permission was given by the physician. The purpose and nature of the study were reviewed and participants were screened for eligibility if there was expressed interest to participate. If women were eligible and interested, they were given two copies of the consent and HIPAA authorization forms in the clinic. After review, participants were asked for verification of understanding of the consent and HIPAA forms, and then asked for signature. One signed copy was given to the participant and the other signed copy was kept by the project staff.

Referrals from other institutions

Institutions affiliated with the Eastern Cooperative Oncology Group (ECOG) referred potential participants and acquaintance controls for the ACS study. In addition, Vanderbilt University investigators referred potential participants for the ACS study. The ECOG Statistical Office identified names of potential participants from a computerized database. The ECOG office contacted the physician at the specific institution associated with the potential participant and the physician was asked to contact the participant about the study. The names of eligible and willing BCS were faxed to a secure location at IUSON. Vanderbilt University also provided study referrals for the ACS using a database of women who had participated in an epidemiological study and who had agreed to be contacted for future studies. The research team from Vanderbilt contacted potential participants regarding the ACS and forwarded eligible and willing BCS.

For both regional recruitment referrals, once the names were received, a letter and study brochure describing the study was sent. After one-week, a study team member from IUSON contacted the potential participant by telephone. Women were screened over the telephone and verbal permission was obtained to send two copies of the informed consent and HIPAA authorization form. Study questionnaire packets were mailed after informed consent was received. Those who received mailed consents from any of the above recruitment methods and did not return a signed consent received a reminder phone call one-week and two-weeks following their initial recruitment date. This telephone call was used to provide additional study information and verify women's interest in participating. If after two additional weeks the consent was not obtained, the study team member mailed a refusal postcard to the potential participant. The postcard was a self-addressed

stamped card that described the purpose of the study and provided a checkbox to mark if the woman did not want to participate in the study. The card was only identified by the study identification number for the purposes of data entry.

Acquaintance control recruitment

Acquaintance controls were recruited by the BCS participants who completed the parent studies. Survivors were asked for names of two (AA) or three (ACS) acquaintances. Specifically, BCS were asked to identify and provide contact information for acquaintances with similar age, gender, education, and race. BCS were asked if the investigators could use the patient's name when contacting acquaintances. The PI of the ACS study (Champion) has successfully used this type of acquaintance-identification techniques for three separate, externally funded studies. Study team members contacted the potential WWBC age-matched control by telephone and explained the purpose of the study. If the WWBC agree to participate, an introductory letter, informed consent statement, and background questionnaire was mailed. If the WWBC was not willing or available to be included in the study, a match was obtained from the pool generated by the other BCS participants.

Protection of human subjects

The Human Research Protection Program at Indiana University-Purdue University Indianapolis (IUPUI) is an accredited site designated by the Association for the Accreditation of Human Research Protection Programs, Inc. It exists to protect the rights and welfare of human research participants recruited to participate in research conducted under the direction of Indiana University.

In keeping with the policies of the Health Insurance Portability and Accountability Act (HIPAA) and Indiana University, the research for both the ACS and AA were reviewed and approved by the IUPUI Institutional Review Board and IUSCC Scientific Review Committee prior to the implementation with human subjects. Several methods were used to protect patient confidentiality. Identifying information was collected on paper forms and entered into a secure database in a limited access folder on the IU School of Nursing (IUSON) server. Once identifying information was entered into the database, paper forms were filed in a locked file cabinet in the investigator's office. Patients were informed of the right to stop participation at any time during the study without penalty or adverse ramifications.

Data collection

For both parent studies, eligible and willing BCS and WWBC who return signed consents were then mailed study questionnaires. Questionnaires were coded with a unique identifier so individuals' information was only linked by identifier in a secure location. When questionnaires were received by study team members, they were visually checked for completeness and logged into a secured computerized database.
If missing items were not complete on the questionnaires, participants were called to determine if this was purposeful or oversight. After this initial data check, all questionnaires for both studies were scanned through an electronic device by the biostatisticians that combined the results into a secure-computerized statistical database. All hard copy forms were returned to the ACS or AA office at the IUSON and filed into locked file cabinets.

If after two-weeks the questionnaire was not returned, the participant was contacted by phone to inquire about questions or problems with the questionnaire. If the questionnaires were not obtained after an additional two weeks, the study team member mailed a refusal postcard to the potential participant. The postcard was a self-addressed stamped card that described the purpose of the card and provided a checkbox to mark if women did not want to participate in the study. The card was only identified by the study identification for the purposes of data entry.

Part 2: Study Dataset for this Study

The second part of this chapter describes the; (1) design, (2) sample criteria, (3) study procedures, (4) measures, and (5) data analysis of the dataset used in this research to evaluate predictors of sleep-wake disturbances in BCS.

Design

A convenience sample was used. The study design was a descriptive, cross-sectional, case-controlled study.

Sample criteria

The sample for this sub-study of sleep-wake predictors in BCS included matched participants with completed questionnaires from one of the parent studies.

Study procedures

Data from the ACS and AA databases were merged into one large database. The database was kept on a secure university computer server using a secure username and password only accessed from the university computer networks.

Age and education-matching

Age-matching was performed by frequencies on birth-date. BCS and WWBC were matched within +/- 5 years of age. For education, BCS and WWBC were matched only if frequencies revealed significant differences in each group. Matching was performed by placing BCS and WWBC into categories of education such as; (a) high school education or less, (b) undergraduate education, or (c) graduate education. A chi-square (education by group) assessed for any significant differences.

Power analysis

The proposed sample size was based on power analyses for research questions 3 and 4. For research question 3, to power for the planned logistic regression, power was based on the ability to predict or detect a rarer outcome. Based on prior studies, 65% of BCS are poor sleepers, thus, 35% were expected to be categorized as good sleepers (rarer outcome) (Carpenter et al., 2004; Elam & Carpenter, 2004a, 2004b; Elam & Carpenter, 2005). For the WWBC group, based on prior studies 50-60% of WWBC were good sleepers, thus, 40-50% were expected to be categorized as poor sleepers (rarer outcome) (Shaver, Giblin, & Paulsen, 1991; Shaver & Zenk, 2000). To detect significant predictors ($p<0.05$) in this study using logistic regression, there needed to be at least five observations per parameter for the rarer outcome for the final regression model (Grimm & Yarnold, 2000). Therefore, if the sample consisted of 242 in each group, 35% of the BCS (n=88) and 50% of WWBC (n=125) would be expected to be good sleepers, which supported the analysis of up to 17 possible predictors in each group.

For research question 4, to power for the multiple regression, there were 10 participants per predictor variable (Tabachnick & Fidell, 2001). Since the study evaluated

17 BCS predictor variables and 14 WWBC predictors, there was a need for at least 170 participants per group of BCS and WWBC.

Based on the largest sample needed to obtain power in this study (research question 3 in the BCS group), the dataset included 246 BCS and 246 WWBC. The ACS study provided a sample of 520 BCS and matched acquaintance controls (WWBC). The AA study completed recruitment with complete data on 133 BCS and 75 WWBC. Combining both studies provided an ample sample for this analysis.

Measures

The following outlines the questionnaires used for this study (see APPENDIX E). Each predictor category was measured using specific items or scores (see Table 2). Not all questionnaires were applicable to the WWBC because they measured experiences specific for breast cancer (see specific items in Table 2). These were analyzed only as unique predictors specific for BCS.

Primary outcome of sleep

The main outcome of sleep was assessed using a subjective questionnaire. The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) was designed for use in clinical populations as a simple and valid assessment of sleep. The tool contains 19-items that produce a global sleep quality score based on 7 component scores: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications, and daytime dysfunction. PSQI items use varying response categories including Likert-type responses. Responses are based on the prior month's habits. Psychometric properties of the PSQI such as internal consistency reliability have been widely supported in a variety of populations (Gentili et al., 1995; Pasternak et al., 1994;

Tiffin et al., 1995), including non-cancer populations (n=52; α=0.83) (Buysse et al., 1989) and BCS (n=102; α=0.80) (Carpenter & Andrykowski, 1998). Construct validity has also been shown in non-cancer populations through convergent validity (r=0.69) and discriminate validity (r<0.37) (Carpenter & Andrykowski, 1998). PSQI global sleep scores, component scores, and PSQI cut-off scores (>5) were used for analyses.

Predictors of sleep-wake disturbance

The four predictor categories from the psychobiological model (see APPENDIX C) included; (a) sample characteristics, (b) physiological, (c) psychological, and (d) environmental predictors.

Sample characteristics.

Demographic data that provided sample characteristics was collected by the Personal Characteristics Questionnaire (PCQ). These are common questions collected from respondents in past research studies and have performed well in cancer patient populations (Giesler et al., 2005). Specifically, the questionnaire assessed items including respondents' age and marital status, educational and income level, employment status, type of medical insurance, and race. Race and ethnicity were assessed using single item measures, but participants had the option of checking multiple categories to best represent the individual's racial or ethnic background. For this study, specific questions from the PCQ were used in the evaluation of person characteristics that potentially predicted poor sleep. Items that assessed age, education, race, and socioeconomic status were evaluated.

In addition, in the BCS group, information about breast cancer and treatment was obtained from abstracting medical records using a standardized form. Data included date

and stage at diagnosis, types and dates of treatment (surgery, chemotherapy, radiation), and endocrine therapy. This information was reported as part of the sample description but information regarding type of treatment (chemotherapy and radiation) and stage of breast disease (stage I, II, III) was used as predictors.

Physiological predictors.

Physiological predictors included co-morbidities, physical symptoms including residual side effects of cancer treatment, and hot flashes.

Co-morbidity information was obtained from the Medical History Questionnaire (MHQ) (Champion).The questionnaire was generated specifically for the ACS study (also administered in the AA study) and provided information that is often not explicit in medical records. The questionnaire consisted of 21-items regarding the presence of disease states and general health. Specifically, the MHQ item #7 provided a total number of co-morbidities for BCS and WWBC. Since this was a general medical history questionnaire, reliability and validity estimates were not available for this tool.

Physical function was measured by the RAND Physical Functioning -10 (PF-10), a valid and reliable 10-item scale that provideed an assessment of overall physical function. The PF-10 is the physical functioning scale of the MOS SF-36 and one of the most commonly used measures of health related quality of life (Haley, McHorney, & Ware, 1994; McHorney, Ware, & Raczek, 1993). Cronbach's alpha coefficient (internal consistency reliability) for the PF-10 generally exceeded 0.90 in research studies (Haley et al., 1994; McHorney et al., 1993). For this study, the total score was used to evaluate the relationship between physical functioning and sleep.

Long-term side effects of cancer were measured using two instruments. First, the Medical Record Audit Form (MRAF), specifically designed for the ACS study (Champion), was used to abstract medical record information from participant charts. The 9-item form was used to collect standard disease and treatment information. Trained study staff extracted data from medical records. Reliability of the extracted data cannot be verified. This form differs from the MHQ in that it was used to obtain specific dates of diagnosis, specific treatment (e.g., type of chemotherapy agents), and specific staging information. Since this was a general medical history questionnaire, reliability and validity are not available for this tool. For this study, besides providing information to describe the sample, items 4, 12, and 13 were used to evaluate the relationship between the type of cancer treatment and sleep, and stage of breast cancer and sleep. This questionnaire was applicable only to the BCS group.

Second, the Symptom Experience Report (SER) has been used in prior research to assess the presence and severity of various symptoms and was used to measure residual and/or current side effects of cancer treatment (Andrykowski et al., 1997; Carpenter, Andrykowski, Cordova, Cunningham, & Studts, 1999; Neugarten & Kraines, 1965). The SER used in the ACS and AA studies evaluated 12 symptoms of lymphedema and neurological symptoms that can occur after treatment, thus, it was only administered to the BCS group. Participants indicated if each symptom occurred in the previous week. For this study, positive responses to individual items/symptoms were summed to obtain a total number of symptoms per subject. This number was used to evaluate the relationship between the long-term side effects of cancer and sleep in BCS. Since this questionnaire

was a symptom checklist, psychometric properties are not available (Nunnally & Bernstein, 1994).

Menopausal symptoms were measured using the 14-item Menstrual and Gynecological History (MGHQ) questionnaire. Information regarding prevalence of hot flashes (item-12 and 13) were obtained from BCS and WWBC and were used to evaluate hot flash frequency. No psychometrics properties have been reported on this inventory since it is a general history questionnaire.

Psychological predictors.

Psychological predictors included general distress (depression and anxiety) and cancer-related distress (concerns of recurrence, intrusive and avoidant thoughts related to cancer).

Depressive symptoms were assessed using the Center for Epidemiologic Studies-Depression Scale (CES-D), a 20-item self-report instrument assessing the presence and severity of depressive symptoms occurring over the past week. (Radloff, 1977). Scores $\geq$ 16 are indicative of high depressive symptoms, but are not considered a diagnosis of clinical depression (Berkman et al., 1986; Comstock & Helsing, 1976). This cut-off point of 16 has been used extensively in other studies, including studies of BCS (Carpenter & Andrykowski, 1998). For this study, total scores were used to evaluate the relationship between depressive symptoms and sleep-wake disturbances. Internal consistency reliability has been shown to be adequate in cancer and non-cancer populations with Cronbach's alpha coefficients of >0.85 (Hann, Winter, & Jacobsen, 1999).

State and trait anxiety were measured using the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Lushene, 1983). The STAI contains two self-report

scales for measuring state and trait anxiety. The S-Anxiety (state) scale includes 20 statements that assess how an individual currently feels, whereas the T-Anxiety (trait) scale includes 20 statements that assess how an individual generally feels. Cronbach's coefficients of the S-Anxiety (state) range from 0.86 to 0.95 while the T-Anxiety ranged from 0.89 to 0.96, depending on the sex and employment status of the population to which it was administered (Spielberger et al., 1983). For this study, both the state and trait total scores were evaluated.

Cancer related distress was measured using 2 scales. First, the Concerns about Recurrence Scale (CARS) (Vickberg, 2003), a two-part instrument developed for breast cancer survivor, evaluated the relationship between concerns of breast cancer recurrence and sleep-wake disturbances. The Likert-type response questionnaire (not associated with time) was given only to the BCS group. The first part consisted of 4 items assessing overall concerns of recurrence; the second part consisted of 29 items grouped into 4 subscales that assess the reasons for anxiety over recurrence. The 4 subscales assess breast cancer recurrence-related worries about death, health, role and womanhood. Internal consistency reliabilities ranged from 0.87 to 0.94 (Vickberg et al., 2003). For this study, total scores of the first part were used to evaluate the relationship between concern of recurrence and sleep-wake disturbances.

Second, the Impact of Events Scale (IES) a 15-item self-report questionnaire, measured cancer-related distress as intrusive and avoidant thoughts about cancer. The IES was designed to assess current subjective distress for any specific life event (Horowitz, Wilner, & Alvarez, 1979). Scoring and subscale reliability has been established with satisfactory internal consistency in non-cancer populations (n=66;

α=0.86 total scale; intrusion α=0.78, avoidance α=0.82). Internal consistency was found to be satisfactory in female populations (n=480 non-cancer women; α=0.91 for total scale; subscale alphas: intrusion α=0.88, avoidance α=0.84) (Thewes, Meiser, & Hickie, 2001) and has been used in breast cancer studies (alpha not reported) (Turner et al., 2005). For this study, the IES intrusion and avoidance total scores were evaluated in both BCS and WWBC to determine the relationship between a stressful life event (breast cancer in the BCS, other event in the WWBC) and sleep-wake disturbances.

Environmental predictors.

Sleep environment predictors were gathered from two questionnaires, the PSQI and the MGHQ. First, information regarding sleep environment was assessed using item 19 on the PSQI, a question that is not used for calculating the total score. This item addresses the presence of a bed partner or roommate (Buysse et al., 1989). Although this was a narrow view of sleep environment, the parent studies did not include a comprehensive questionnaire regarding specific environment issues or sleep hygiene (see Chapter Five). Second, information regarding presence of children in the home was gathered from item #7 in the MGHQ. The question asks if children are living with the participant at the present time. This provided information regarding child rearing that can create a disrupted sleep environment.

Table 2

List of Measures

Variable		Measure	Item/ score	Level of measurement	Range of scores	Validation in BCS	Validation in WWBC	RQ(s)*
Outcome	Sleep presence of sleep disturbances	PSQI	Global scores (based on items 1-18) are compared to standardized cutoff scores	Categorical	Dichotomous above or below cutoff	Yes	Yes	1
	Sleep severity of sleep disturbances	PSQI	Global score (based on items 1-18)	Continuous	0-21	Yes	Yes	2
Predictor								
Person	Age	PCQ	#13	Continuous	n/a	n/a	n/a	3,4
	Education	PCQ	#7a	Continuous	n/a	n/a	n/a	3,4
	Race	PCQ	#9	Categorical	n/a	n/a	n/a	3,4
	SES Income	PCQ	#12	Categorical	n/a	n/a	n/a	3,4
	Employment	WI	#6	Categorical	n/a	n/a	n/a	3, 4
	Menopausal status	MGHQ	#2	Categorical	21	n/a	n/a	3, 4
Physiological								
	Co-morbidities	MHQ,	Total score based on item #7	Categorical	0-19	n/a	n/a	3, 4

Variable		Measure	Item/ score	Level of measurement	Range of scores	Validation in BCS	Validation in WWBC	RQ(s)*
		PSS [1]	Total score based on items #2, 3, or 6 added to MHQ total score	Categorical	True/false	n/a	n/a	3, 4
	LT s/e of cancer tx							
	Type of cancer tx	MRAF [1]	#4, 12, 13	Continuous, Categorical	n/a	n/a	n/a	3, 4
	Long-term side effects	SER[1]	Total severity	Continuous	0-48	Yes (longer version)	Yes	3, 4
	Post-menopausal symptoms (HF's)	MGHQ	# 12, 13, 14	Categorical	n/a	n/a	n/a	3, 4
	Physical functioning	PF-10	Total score	Continuous	10-30	Yes	Yes	3, 4
Psychological	Cancer related distress	CARS [1]	Total scores on part 1-3	Continuous	4-24 (part 1)	Yes	n/a	3, 4
	General psychological distress							
	Depression	CES-D	Total score	Categorical	0-60	Yes	Yes	3, 4
	Anxiety	STAI	Total score for both state and trait	Categorical	20-80 (Y-1) 20-80 (Y-2)	Yes	Yes	3, 4

Variable		Measure	Item/ score	Level of measurement	Range of scores	Validation in BCS	Validation in WWBC	RQ(s)*
	Distress r/t life event	IES	Total score for both intrusion and avoidance	Categorical	0-35 (intrusive) 0-40 (avoidance)	Yes	Yes	3, 4
Environment	Companion/bed partner	PSQI	#19	Categorical	See above			3, 4
	Family developmental stage	MGHQ	#7	Categorical	See above			3, 4

*=Research question, 1=measured only in BCS

Data acquisition and preparation

Permission was granted to obtain electronic copies of the parent datasets by the principal investigators for each study. Datasets were received through a password-protected file folder stored on a secure data server to maintain confidentiality of data. The datasets were received in Statistical Package for the Social Sciences (SPSS) (v. 15.0) (Chicago, IL) format. The parent datasets contained questionnaires completed by BCS and WWBC. It was established that the sample size of both parent datasets provided sufficient numbers of subjects to proceed with age-matching. Data was examined by case summaries to detect missing items within each questionnaire. This section provides details of the following procedures; (a) subject matching, (b) data cleaning, and (c) reliability of questionnaires.

Subject matching

The secondary dataset was established by matching BCS and WWBC through visual examination of frequency data by age. A pool of 520 BCS and 252 WWBC were identified from the parent datasets. A total of 246 BCS were matched within +/-5 years of age with 246 WWBC (n=492). A chi-square test for independence showed that levels of education were not significantly different between BCS and WWBC ($\chi^2(2)=4.73$, $p=0.09$) suggesting that the groups were also education-matched.

Of the BCS included in the analysis, 148 were recruited by telephone or local clinic referrals (Indiana University Cancer Clinic and Wishard Memorial Hospital) and 98 from other institutions outside of Indiana (ECOG institutions including Vanderbilt University). The recruitment location was not recorded for the WWBC. However, of the

women included, 173 were from the ACS study and 73 from the AA study. Only subjects that submitted completed questionnaires were considered for this analysis.

Data cleaning

Completed questionnaire packets from each parent study were checked twice prior to data entry. For both studies, missing items were addressed by attempting to contact subjects by telephone. If the contact was successful, subjects were asked to verbally reply to the missing items. If this was not successful, the packets were forwarded with missing data to the data management team for scanned entry into a computerized database. After scanning, missing items were checked to ensure the scanning process was not the reason for missing items. Although completeness of standardized questionnaires was evaluated by parent study team members, there were some missing values in the secondary dataset.

Data cleaning was performed. First, total or mean scores were calculated for each questionnaire used in the parent studies. Next, descriptive and frequency statistics examined overall patterns of missing values for the new total/mean scores. The second step in data cleaning was to examine individual missed items. This was completed through frequencies and case summaries by the subject identification number. Patterns of missing items were evaluated by subject to determine any patterns within group (BCS or WWBC) and/or by subject. Missing data were found to be randomly distributed by subject and item/questionnaire. One subject was identified with several missing items and was subsequently replaced with a different age-matched subject. Overall, the amount of missing data was calculated to be 1.07% of the entire dataset which is relatively low for a large dataset (Tabachnick & Fidell, 2001).

After evaluation of the secondary dataset, decisions regarding the best method to resolve the missing items were made and can be found in APPENDIX F. For missing mean or total scores, mean imputations were completed based on group and race. After imputations were completed, frequencies and descriptive statistics were repeated to ensure all values were present. Mean or total scores for each continuous questionnaire scale were recalculated based on the imputed items. Frequencies and descriptive statistics were repeated to ensure all subjects had complete data.

During the cleaning process it was found that one of the parent studies did not include the measure of anxiety (State and Trait Anxiety Inventory). This prompted a preliminary examination of multicollinearity between anxiety and other psychological measures. Correlations revealed that the CES-D was highly correlated with state anxiety ($r=0.67$, $p=0.00$) and trait anxiety ($r=0.75$, $p=0.00$) suggesting collinearity between depression and anxiety. Since the CES-D was given in both parent studies, it was used in the analyses. The STAI was not included in the analyses.

Reliability analysis

The third step in data preparation was to examine the internal consistency reliability of each standardized questionnaire per group and in the combined sample using Cronbach's alpha coefficients. Single item variables were not included in this analysis. In addition, the Symptom Experience Report (SER) was excluded from the analysis since the responses were dichotomous yes/no options that determined the number of symptoms present. Since this questionnaire is considered a checklist for cancer related symptoms, the items are not linked and would not produce a meaningful internal consistency reliability statistic (Nunnally & Bernstein, 1994). For questionnaires that produce a total

score (CES-D and CARS), the individual items were entered (Nunnally & Bernstein, 1994). For questionnaires that produced sub-scales (PSQI, IES), the subscales rather than items were entered into the analysis. The rationale for this method is that the subscales which include the items provide a more accurate measure of internal consistency (Nunnally & Bernstein, 1994). In addition, for the PSQI, the sleep disturbance subscale items were evaluated to determine if the subscale was internally consistent.

Cronbach's alpha coefficients greater than 0.80 were desired for this analysis since the study used established measures (Polit & Hungler, 1999). Results found in Table 3 showed an acceptable range of alpha coefficients per group and in the combined sample establishing adequate internal consistency reliability of measures except for the Pittsburgh Sleep Quality Index and CES-D (BCS only). This suggests that most measures captured the critical attributes of the variable of interest in each group and in the combined sample (Polit & Hungler, 1999).

Table 3

Estimates of Internal Consistency Using Cronbach's Alpha Coefficients

		Alpha Coefficient				
Scale	# items	BCS (n=246)	WWBC (n=246)	Combined Sample (n=492)	Caucasian (n=342)	Minority (n=150)
Pittsburgh Global Sleep Score [1]	7	0.73	0.73	0.74	0.74	0.73
Pittsburgh Sleep Disturbances Items	9	0.73	0.78	0.76	0.68	0.80
Physical functioning (PF-10)	11	0.93	0.93	0.93	--	--
Concerns about recurrence [2]	4	0.89	n/a	n/a	--	--
CES-D [3]	20	0.76	0.83	0.79	--	--
Impact of Events Scale [4]	20	0.92	0.94	0.94	--	--

1=evaluated the 7 component scores, 2=only given in BCS, 3=Center for Epidemiologic Studies on Depression Scale, 4=evaluated revised subscales of intrusion and avoidance

In sum, a secondary dataset was created from two parent datasets matching BCS and WWBC women within +/- 5 years of age. A sample of 492 women was established providing ample sample size to address the four research questions. Missing data were evaluated and resolved. Finally, standardized measures used in the secondary dataset were evaluated for internal consistency reliability. All multi-item measures had adequate reliability to proceed with data analysis.

Data analysis

Data consisted of a single set of observations. Data analyses were performed using SPSS (v. 15.0, SPSS Inc., Chicago, IL). The following address the statistical analysis performed for each research question. Demographic variables were evaluated using descriptive and frequency statistics. Groups were compared using independent t-

tests and chi-square. If group differences arose, variables were controlled for during analysis.

Research question 1

To answer research question 1, "Is there a difference in the prevalence of sleep-wake disturbances between women surviving breast cancer compared to age-matched WWBC?" the following analysis was performed. First, a new variable was created using the PSQI global scores. Based on the established cut-off scores in the literature, women who scored >5 were coded as "yes" for sleep-wake disturbances. All others were coded as "no". The two groups were compared using a logistic regression to control for group differences in demographic characteristics. Percentages of women who scored above the cut-off (e.g., poor sleepers) were reported.

Research question 2

To address research question 2, "Is there a difference in the severity of sleep-wake disturbances between BCS compared to age-matched WWBC?" analysis of covariance was used to control for variables such as group differences in demographic characteristics. Pittsburg Sleep Quality Index global scores and seven PSQI component scores were compared between groups using ANCOVA.

Research question 3

To address research question 3, "What are the physiological, psychological, and environmental predictors of poor sleep (defined by PSQI score >5) in BCS and age-matched WWBC?" logistic regression was performed using three steps. The first step evaluated the relationship among all of the person characteristics, physiological, psychological, and environmental predictors (independent variables). Each predictor was

placed into categorical groups based on the frequencies for each individual predictor. To start, if the number of subjects scoring above and below the established cut-off (if applicable) was near the median, the cut-off was used to split the group into two categories (e.g., depressed or non-depressed). If there was no established cut-off, or the outcome was skewed, the median was used to split the predictor by a standard increment of the measure to obtain adequate representation per group (either median split or quartiles).

The second step included chi-square analyses between each predictor and the outcome of sleep to determine how each predictor related to the occurrence of poor sleep. Relationships were considered significant with a $p \leq 0.25$ and were entered into the final regression model (Hosmer & Lemeshow, 2000).

In the third step, all significant predictors were entered into the final logistic regression model. Significant relationships between sleep and the individual predictors were based on odds ratios with a 95% confidence interval outside of 1.0 and $p<0.05$ (Tabachnick & Fidell, 2001).

Research question 4

To address research question 4, "What are the physiological, psychological, and environmental predictors of sleep-wake disturbances (using PSQI global scores) of BCS and age-matched WWBC?" multiple regression was performed using three steps.

For the first step, the investigator compared relationships between each individual variable (predictor) and PSQI global sleep scores. When variables were continuous, Pearson correlations were used to determine relationships between the dependent and independent variable (e.g., sleep and depression). Pearson correlations greater than $r=|0.2|$

with $p \leq 0.25$ were considered significant and these variables were placed into the final regression equation (Hosmer & Lemeshow, 2000). If the independent variable was categorical, a t-test was used to determine if the variable was related to PSQI global sleep scores (Munro & Page, 1993; Tabachnick & Fidell, 2001). Since this was an exploratory regression to find initial information on predictors of sleep, the r-value and p-value's set for inclusion were broad in order to allow for a comprehensive set of predictors to be evaluated.

In the second step, all of the significant predictors from step two were entered into the final regression model. Model fit for the regression was verified. In addition, the p-value of each independent variable was evaluated to determine if that individual predictor significantly improved the fit of the model. If the fit was worse when that variable was omitted from the model (the p-value would be low), therefore, the variable had a significant impact on the model (Munro & Page, 1993). Significant relationships between sleep and the individual predictors were based on $p<0.05$.

In sum, sleep-wake disturbances in BCS are a significant problem. Few studies have evaluated a comprehensive set of predictors of sleep-wake disturbances in BCS. Therefore, this analysis evaluated a comprehensive set of predictors to determine the occurrence and severity of sleep-wake disturbances in BCS compared to WWBC. Finding unique predictors in BCS provides further evidence and support for a unique theoretical model.

CHAPTER FOUR

RESULTS

The purpose of this research study was to gain further knowledge regarding the incidence, prevalence, and predictive factors of sleep-wake disturbances in BCS compared to age-matched WWBC. This chapter contains data analyzed from quantitative questionnaires from two quality of life studies that included BCS and WWBC. The chapter focuses on the statistical analyses including sample characteristics and the goals of the secondary data analyses which were to determine; (1) if the presence of sleep-wake disturbances was different between BCS and age-matched WWBC, (2) if the severity of sleep-wake disturbances was different between BCS and age-matched WWBC, (3) the physiological, psychological, and/or environmental predictors of sleep-wake disturbances in BCS and age-matched WWBC, and (4) if these predictors were different between BCS and age-matched WWBC.

Statistical Analysis

Sample characteristics of BCS and WWBC

In the BCS group, disease and treatment variables are reported using descriptive and frequency statistics in Table 4. Demographic variables including age, education, race/ethnicity, marital status, income, work status, number of non-cancer health co-morbidities, and menopausal status were evaluated using descriptive and frequency statistics for BCS and WWBC as listed in Table 5. Both groups had a mean age of 48 years and at least a college education. The groups were mainly Caucasian, non-Hispanic or Latino, and married or partnered. Over 70% had incomes over $50,000 with a majority

working full or part-time. Both groups reported at least 2-3 co-morbid conditions (excluding cancer diagnosis in BCS) and more BCS reported to be post-menopausal compared to WWBC.

Group differences were evaluated using independent t-tests and chi-square tests for independence. Results showed no significant differences on age using an independent t-test presented in Table 4. Using chi-squared tests of independence, no differences were found between BCS and WWBC on education (high school or less, college, graduate), ethnicity (Hispanic/ Latino or not) marital status, (partnered, no partner), income (below $50,000 and above $50,000), work status (full-part time, no work), number of non-cancer health co-morbidities (yes or no). Group differences were noted for race (Caucasian, black, other) and menopausal status (pre-menopausal, post-menopausal) and will be addressed in each research question below.

Table 4 Demographic and Health Characteristics of Subjects

	BCS (n=246) M (SD)	WWBC (n=246) M (SD)	p
Age (years)	48.21 (8.50)	48.26 (10.39)	0.94
	% (n)	% (n)	p
Level of education			
High school or less	26 (64)	23 (57)	0.09
College or trade	59 (144)	54 (132)	
Graduate	15 (38)	23 (57)	
Race			
Caucasian	76 (186)	63 (156)	0.01*
African American	20 (50)	33 (81)	
Asian	1 (2)	1 (2)	
American Indian		1 (2)	
Other	3 (8)	2 (5)	
Ethnicity			
Hispanic or Latino	2 (4)	4 (9)	0.13
Not Hispanic or Latino	98 (242)	96 (237)	
Marital status			
Married/living with partner	73 (180)	62 (153)	0.07
Divorced or widowed	12 (29)	13 (31)	
Single	14 (35)	24 (58)	
Other	1 (2)	1 (4)	
Household income in $ (SES)			
≤15,000 per year	11 (27)	15 (37)	0.18
15,001-30,000 per year	13 (32)	8 (20)	
30,001-50,000 per year	15 (37)	22 (54)	
50,001-100,000 per year	36 (89)	32 (79)	
≥ 100,001 per year	25 (61)	23 (56)	
Employment status			
Working full	52 (128)	48 (118)	0.07
Working part-time	21 (52)	16 (39)	
Unemployed	18 (44)	23 (57)	
Retired	9 (21)	10 (25)	
Student	0 (1)	3 (7)	
Reporting non-BC co-morbidities			
None	3 (7)	7 (18)	0.09
1 condition	43 (106)	44 (108)	
2-3 conditions	35 (87)	33 (80)	
4 or greater conditions	19 (46)	16 (40)	
Menopausal status			
Pre-menopausal	30 (73)	47 (115)	0.00*
Post-menopausal	70 (173)	53 (131)	

*p≤0.01. All values based on valid percentages and rounded to nearest tenth

Characteristics of the type of breast cancer and treatment were evaluated and can be found in Table 5. Results showed a majority of BCS received surgery (100%) and chemotherapy (89%) for non-metastatic disease (stage I-III), and had not taken hormone modulators such as tamoxifen (67%). The mean time since diagnosis was 5.62 years.

Table 5

Breast Cancer Disease and Treatment Information

	BCS (n=246) M(SD)
Time since diagnosis (years)	5.62 (2.03)
	% (n)
Surgery	
Lumpectomy	42 (102)
Mastectomy	59 (144)
Chemotherapy	
Received some chemotherapy	89 (211)
Received no chemotherapy	11 (35)
Use of hormone modulator	
Never taken	67 (331)
Current use	9 (43)
Past use	24 (118)

Results of standardized questionnaires

The following are the results of the standardized questionnaires for each group (see Table 6). Significant differences between BCS and WWBC scores were noted for the PSQI, CES-D, and IES. BCS mean scores were higher for the global sleep score and CES-D compared to WWBC. However, WWBC had higher impact of a life event noted by higher mean scores for the IES.

Table 6

Results of Standardized Questionnaires

Scale	Results		
	BCS M(SD)	WWBC M(SD)	p
PSQI Global Score	7.31 (3.80)	5.80 (3.45)	0.00*
Physical functioning (PF-10)	2.55 (0.51)	2.62 (0.49)	0.15
Symptom experience report[1]	3.74 (3.62)	----	----
Concerns about recurrence[1]	12.15 (5.51)	----	----
Center for Epidemiological Studies Depression Scale (CES-D)	11.53 (9.60)	9.00 (9.20)	0.00*
Impact of Events Scale (IES)	1.50 (1.23)	1.86 (1.36)	0.00*

*p<0.05, 1=BCS measure only

Research question 1

To answer research question 1, "Is there a difference in the prevalence of sleep-wake disturbances between women surviving breast cancer compared to age-matched WWBC?" a chi-square test of independence and a logistic regression were performed.

The first step in this analysis was to create a new variable based on the established global sleep score (>5) from the Pittsburgh Sleep Quality Index (PSQI) to distinguish between good and poor sleepers. In the second step, chi-square tests of independence were performed to determine if good/poor sleep was significantly related to race and menopausal status to determine if these needed to be controlled in the analysis. Results showed that both race ($\chi^2(1)=8.63$, p=0.02) and menopausal status ($\chi^2(1)=28.17$, p=0.00) were significantly related to sleep. Thus, these were controlled in the analysis for research question 1.

A crosstabulation analysis was performed to determine the number of poor sleepers per group, race and menopausal status. Results showed that 65% of BCS and

55% of WWBC scored at or above the cut-off for poor sleep quality. In addition, more Caucasian ($\chi^2(1)=4.45$, p=0.04) and postmenopausal ($\chi^2(1)=16.96$, p=0.00) women scored above the cut-off for poor sleep quality.

Since there were differences in sample characteristics related to the variable of good vs. poor sleep, a logistic regression was performed to control for sample characteristics. No prior assumptions were examined regarding distributions since normality, linearity, and equal variance are not factors for this type of regression (Tabachnick & Fidell, 2001). The independent variables were coded in dichotomous categories to facilitate interpretation of results (Tabachnick & Fidell, 2001). The binary logistic regression revealed that BCS were 1.96 times more likely to be poor sleepers compared to WWBC (p<0.01) when controlling for race and menopausal status (listed in Table 7).

Table 7

Logistic Regression to Determine Prevalence of Poor Sleep by Group

	B	p	OR	95% CI	
				Upper	Lower
Group [1]	0.67	0.00*	1.96	1.31	2.92
Race [2]	0.50	0.03*	1.65	1.06	2.56
Menopausal status [3]	0.60	0.00*	1.82	1.23	2.71
χ^2	38.06				
df	3				
p	0.00				

1=BCS vs. WWBC, 2=Caucasian vs. all other, 3=Premenopausal vs. postmenopausal, overall model statistic $\chi^2(3)=38.06$, p<0.00)

In summary, the prevalence of sleep-wake disturbances was significantly different between BCS and WWBC. BCS were more likely to experience sleep-wake disturbances compared to WWBC.

Research question 2

To answer research question 2, "Is there a difference in the severity of sleep-wake disturbances between women surviving breast cancer compared to age-matched WWBC?" the continuous dependent variables of sleep (PSQI global score and 7 component scores) were evaluated between groups using an independent t-test. Since there were group differences in race and menopausal status, analysis of covariance (ANCOVA) models were performed to control for these variables. The ANCOVA was selected over multivariate analysis of covariance (MANCOVA) since group, race and menopausal status were not significantly different for each dependent variable of sleep, thus, each variable of sleep was evaluated separately to control only for those relationships that were significant. In addition, since this question focused on differences in severity between BCS and WWBC when controlling for race and menopausal status, only group differences in sleep are presented below. These variables (race and menopausal status) will be addressed in research questions 3 and 4 when evaluating possible predictors of sleep-wake disturbances.

First, covariates were determined through examination of means using independent t-tests of sleep variables for group, race, and menopausal status. Results showed significant group differences (BCS vs. WWBC) for global sleep scores, sleep quality, sleep latency, sleep disturbance, and daytime dysfunction ($p<0.01$). Results also showed significant group differences by race for global sleep scores, sleep quality, sleep latency, sleep duration, sleep disturbance, and sleep efficiency ($p<0.01$) and by menopausal status for global sleep score, sleep quality, sleep latency, sleep disturbance, sleep medication, and sleep efficiency ($p<0.01$).

Based on the above findings, the ANCOVA analysis was performed. However, for daytime dysfunction, a one-way analysis of variance (ANOVA) was performed since this variable was not significantly different by race or menopausal status. Group was the independent variable in the ANCOVA (BCS, WWBC) and race and/or menopausal status were considered covariates. Prior to the analysis, assumptions were evaluated and showed no violations of normality of sampling distributions, linearity, homogeneity of variance, homogeneity of regression, and reliability of covariates.

After adjusting for covariates as appropriate, group differences in the severity of sleep disturbances were noted (Table 8). BCS had higher PSQI scores indicating poorer sleep quality and higher sleep disturbances. ANCOVA results showed that compared to WWBC, BCS had significantly poorer overall sleep quality (global scores) with subscales indicating poorer sleep quality, longer sleep latency, less sleep duration, greater sleep disturbance, and more daytime dysfunction when controlling for race and/or menopausal status. Use of sleep medications and sleep efficiency were not significantly different between groups.

Table 8

ANCOVA Tests for Differences in PSQI Sleep Scores for BCS and WWBC

Variable	Adjusted Mean (BCS)	Adjusted Mean (WWBC)	F	p
Global sleep score[1]	7.26	5.85	17.87	0.00*
Sleep quality[1]	1.20	0.85	25.24	0.00*
Sleep latency[1]	1.39	1.00	14.69	0.00*
Sleep duration[2]	0.98	0.84	4.65	0.03*
Sleep disturbance[1]	1.50	1.31	11.21	0.00*
Sleep medication[3]	0.65	0.61	0.15	0.70
Daytime dysfunction[4]	0.96	0.70	16.9	0.00*
Sleep efficiency[1]	0.59	0.57	0.09	0.77

1=controlling for race and menopausal status, 2=controlling for race only, 3=controlling for menopausal status only, 4=no control variables-ANOVA performed

Since global scores and 5 of 7 component scores (six sleep variables) were significantly different between BCS and WWBC after adjusting covariates, correlations were performed to determine if there were significant relationships between global sleep quality scores and corresponding component scores. The purpose was to determine if the component scores should be considered as separate measures of sleep for research questions 3 and 4. As expected, Pearson correlations showed strong-to-moderate relationships between global sleep scores and the seven subscales presented in Table 9. Based on these relationships, only the global sleep score from the PSQI was evaluated for research questions 3 and 4 since this variable incorporates all of the subscales and best represents the overall measurement of sleep.

Table 9

Pearson Correlation Coefficients for Global Sleep Quality Score with 7 Component Scores

	Global sleep score
Global sleep quality	0.77*
Sleep latency	0.75*
Sleep duration	0.59*
Sleep disturbance	0.63*
Sleep medications	0.56*
Daytime dysfunction	0.50*
Sleep efficiency	0.63*

*$p<0.01$

In summary, chi-square tests indicated the need to control race and menopausal status in some analyses. Sleep variables were evaluated using ANCOVA and ANOVA statistics and revealed that the sleep-wake disturbances were more severe in BCS compared to WWBC. Sleep quality, latency, duration, disturbance, and daytime dysfunction, when controlling for race and/or menopausal status, were significantly worse in BCS than WWBC. Finally, Pearson correlations showed that global sleep scores had strong to moderate relationships with all component scores which indicated that only one sleep variable (e.g., global scores) could be used for subsequent analyses. In the next section, a set of comprehensive variables from the Elam Psychobiological Model are examined to determine which variable(s) contribute(s) to the occurrence of sleep-wake disturbances in BCS and WWBC.

Research question 3

To answer research question 3, "What are the physiological, psychological, and environmental predictors of poor sleep (defined by PSQI scores >5) in BCS and age-matched WWBC?" logistic regression was performed using three steps; (1) creation of dummy variables, (2) determine relationship between sleep and predictors, and (3) perform models of logistic regression. For logistic regression, there are no statistical assumptions such as normality, linearity, and equal variance within groups prior to analysis (Tabachnick & Fidell, 2001) eliminating several steps compared to multiple regression.

Step 1: Creation of dummy variables

To begin, the first step in establishing a list of predictors for sleep-wake disturbances was to determine the relationships among the person characteristics, physiological, psychological, and environmental predictors (independent variables) to be examined from the Elam Psychobiological Model. This was accomplished by creating new variables based on the number of members scoring above and below the standard cut-off scores (if applicable) for each questionnaire as shown in Table 10. If the cut-off score was near the median, the cutoff score was used to split the group into two categories (e.g., depressed or non-depressed). If there was no established cut-off, the median was used to split the predictor by a standard increment of measure to obtain adequate representation per group (either median split or quartiles) (Field, 2005; Tabachnick & Fidell, 2001).

Table 10

Recoding of Variables for Logistic Regression

Variable	Measure	Range of scores	Variable split	n
Sleep	PSQI	0-21	Based on cut-off for measure	
			Group 1=good sleepers ≤ 5	222
			Group 2=poor sleepers >5	270
Group	n/a	n/a	Group 1=WWBC	246
			Group 2=BCS	246
Age	PCQ	28-80	Based on median split	
			Group 1=27-48 yrs	255
			Group 2=49-80 yrs	237
Education	PCQ	n/a	Based on level of education	
			Group 1=high school or less	121
			Group 2=college education	276
			Group 3=graduate education	95
Race	PCQ	n/a	Based on race category	
			Group 1=Caucasian	342
			Group 2=Minority	150
SES status	PCQ	n/a	Based on income categories	
			Group 1=≥$50,001 or more	
Income			Group 2=≤$50,000 per year or less	285 207
Work status		n/a	Based on employment status	
			Group 1=Works full- or part-time	337 155
			Group 2=Does not work	
Menopausal status	MGHQ	n/a	Based on last menstrual period	
			Group 1=Premenopausal (period within 12 months)	204
			Group 2=Post menopausal (no period within past 12 months)	288
Co-morbidities	MHQ	n/a	Based on presence co-morbidities	
			Group 1=0-1	214
			Group 2- Two or more	253
Type of cancer treatment	MRAF [1]	n/a	Based on medical records	
			Group 1=Chemotherapy only	0
			Group 2=Surgery only	35
			Group 3=Chemotherapy plus surgery	211

Variable	Measure	Range of scores	Variable split	n
Long-term side effects	SER[1]	0-12	Based on quartiles of # of symptoms	
			Group 1=0-2 symptoms	121
			Group 2=3-5 symptoms	59
			Group 3=6-12 symptoms	66
Post-menopausal symptoms (Hot flashes)	MGHQ	n/a	Based on presence of hot flashes	247
			Group 1=No hot flashes	245
			Group 2=Yes hot flashes	
Physical functioning	PF-10	10-30	Mean split	
			Group 1=10-25	336
			Group 2=25-30	156
Cancer related distress	CARS [1]	4-24 (part 1)	Based on quartile 25, 50, 75 to get equal distribution	
			Group 1=Scores 4-8	81
			Group 2=Scores 9-11	43
			Group 3=Scores 12-24	122
Depression	CES-D	0-60	Based on cut-off score for depressive symptoms $\geq$ 16	
			Group 1=no depressive symptoms	382
			Group 2=depressive symptoms	110
Distress r/t life event	IES	Mean of 2 subscales (intrusion, avoidance)	Based on the quartiles	
			Group 1=0	28
			Group 2=1-2	390
			Group 3=3-above	74
Bed partner	PSQI item 19	n/a	Based on companion in bed	
			Group 1=No companion	180
			Group 2=Yes companion	312
Children in the home	MGHQ		Based on presence of children in the home	
			Group 1=No children	230
			Group 2=Yes children in the home	262

1=variables only for BCS, n/a=not applicable

Evaluation of variables

Crosstabulation analyses revealed adequacy of the observed and expected frequencies for each of the independent variables after the creation of the dummy variable. This step established that no table had more than 20% of cells with frequencies less than 5, thus, the goodness-of-fit criteria for the model were not violated (Tabachnick & Fidell, 2001).

Step 2: Relationships among sleep and predictors

The second step of research question 3 evaluated chi-square tests of independence between individual independent variables and the outcome of sleep. Relationships with a $p \leq 0.25$ were considered significant and entered into the final regression model (Hosmer & Lemeshow, 2000). This liberal p-value was to allow for marginal relationships in the exploratory evaluation of variables. Results of the chi-square tests showed significant bivariate associations between sleep and group, race, menopausal status, presence of at least one co-morbid condition, presence of hot flashes, level of physical functioning, long-term effects of cancer, depressive symptoms, impact of a life event, presence of a bed partner, and having children in the home (Table 11).

Table 11

Associations Between Dichotomous PSQI Global Score and Predictors

	df	χ^2	p
Group	1	20.52	0.00*
Age	1	1.16	0.28
Education	2	1.42	0.49
Race	1	4.45	0.04*
Income	1	13.74	0.06*
Work status	1	0.00	0.99
Menopausal status	1	16.96	0.00*
Co-morbidities	1	5.57	0.02*
Type of cancer treatment[1]			
Treatment type	1	0.21	0.66
Hormone use	1	0.01	0.92
Hot flashes	1	36.24	0.00*
Physical functioning	1	39.76	0.00*
Long term effects of cancer[1]	2	9.79	0.01*
Concerns about recurrence (cancer related distress)[1]	2	1.59	0.45
Depressive symptoms	1	39.55	0.00*
Impact of life event	2	8.56	0.01*
Having a bed partner	1	2.79	0.10*
Children in the home	1	1.55	0.21*

1=BCS only, *$p \leq 0.25$

The percentage of poor sleepers and mean global scores for each of the significant predictors included in the logistic regression are shown below (see Table 12).

Table 12

Percentages of Poor Sleep and Mean Global Scores for Significant Variables

Variable		Poor sleep[2] (%)	Global score M(SD)
Group	BCS	65	7.31 (3.8)
	WWBC	55	5.80 (3.5)
Race	Caucasian	52	6.18 (3.5)
	Minority	63	7.40 (4.0)
Income	$50,000 or less	64	7.40 (4.0)
	$50,001 or more	49	5.95 (3.0)
Menopausal status	Pre-menopausal	44	5.62 (3.3)
	Post-menopausal	63	7.22 (3.8)
Co-morbidities	0-1	46	5.59 (3.2)
	2 or more	65	7.56 (3.5)
Hot flashes	Yes	67	7.59 (3.4)
	No	43	5.53 (3.7)
Physical functioning	10-25	76	8.31 (3.8)
	26-30	45	5.74 (3.4)
Long term effects of cancer[1]	0-2 symptoms	56	6.39 (3.4)
	3-5	64	7.34 (3.8)
	6-12	76	8.98 (3.9)
Depressive symptoms	Yes	85	9.40(3.9)
	No	46	5.94 (3.9)
Impact of life event	0 score	36	5.21 (3.4)
	1-2	53	6.28 (3.5)
	3-above	73	8.46 (4.5)
Having a bed partner	Yes	52	6.16 (3.4)
	No	61	7.24 (3.1)
Children in the home	Yes	52	6.24 (3.5)
	No	59	6.92 (3.3)

1=BCS only, 2=PSQI global scores >5

Step 3: Models of logistic regression

Step three evaluated all above variables that had significant associations ($p \leq 0.25$) with sleep in a logistic regression model. Of the three possible types of logistic regression (direct, sequential, stepwise), direct entry was performed so that all slated variables were evaluated simultaneously. This method was preferable since there were no initial hypotheses about importance or order of independent variables (Tabachnick & Fidell, 2001). All variables entered were dichotomous or categorical with no more than 3 categories present for one variable. The categories were coded as 0 for the reference group and 1 as the response group for the comparison. Results are evaluated in terms of (1) multicollinearity among variables, (2) test of overall model, (3) test of individual predictors, and (4) interpretation of residuals.

Multicollinearity

Although not an assumption of logistic regression, multicollinearity can have an impact on logistic regression posing a problem with biasing effect among variables (Field, 2005). For logistic regression, collinearity diagnostics were performed by evaluating tolerance and variance inflation factor values (VIF) using linear regression statistics in SPSS (Field, 2005). Results found in Table 13 suggests that there were no issues with collinearity between sleep and predictor variables since tolerance levels were greater than 0.10 and VIF values were less than 10 (Field, 2005). Additional collinearity diagnostics supported these findings through examination of eigenvalues of scaled, uncentered cross-products, condition indexes, and variance proportions for each predictor. Eigenvalues and condition indexes were consistent, meaning that regression parameters would not be affected by changes in the predictors (Field, 2005). Lastly, the

variance proportions, or the variance of each regression coefficient, did not show any predictors with high proportions and small eigenvalues, thus supporting the lack of collinearity (Field, 2005).

Table 13

Test for Multicollinearity of Logistic Regression Variables

Variable	Tolerance	VIF
Group	0.64	1.56
Race	0.71	1.41
Income	0.63	1.60
Menopausal status	0.74	1.35
Co-morbid conditions	0.81	1.24
Hot flasher	0.88	1.13
Physical functioning	0.64	1.56
Symptoms after cancer	0.78	1.28
Depressive symptoms	0.77	1.30
Impact of life event	0.83	1.21
Presence of bed partner	0.67	1.49
Children living at home	0.84	1.19

Three separate logistic regression models were performed. The first model included all predictors to determine which variables accurately predicted the presence of poor sleep. The second model was specific for BCS and included type of cancer treatment and long-term effects of cancer treatment. The third model was specific for WWBC only. The logistic regression output provided inferential tests of the overall models and goodness-of-fit tests of individual variables (Tabachnick & Fidell, 2001).

Test of overall models

Goodness-of-fit tests indicated the statistical models fit the set of observations (Field, 2005). Goodness-of-fit is based on how accurately the data predicted by the regression model is related to the collected data (Field, 2005). If there is no difference

between a model with the slated variables and a model without the variables, then those variables entered have no influence on the dependent variable (Field, 2005). This is an important assumption of regression and must be established before further evaluation of the findings can be completed.

Results showed adequate goodness-of-fit for model 1 ($B=0.20$, $SE=0.09$, $p<0.05$), model 2 ($B=0.62$, $SE=0.13$, $p<0.00$), and model 3 ($B=.21$, $SE=0.13$, $p<0.05$) (Field, 2005; Tabachnick & Fidell, 2001) based on the significant values of the constants. This suggested that the addition of one or more of the independent variables into the regression would significantly change the predictive power (Field, 2005). In addition, chi-square tests of goodness-of -fit (Hosmer-Lemeshow) were not significant for model 1 ($\chi2(8)=10.17$, $p=0.25$), model 2 ($\chi2(8)=5.20$, $p=0.74$), or model 3 ($\chi2(8)=11.07$, $p=0.20$) which is optimal (Field, 2005). The output also showed that the residual chi-square statistic for model 1 ($\chi2(12)=122.35$, $p<0.00$), model 2 ($\chi2(12)=62.24$, $p<0.00$), and model 3 ($\chi2(11)=61.73$, $p<0.00$) suggested that the coefficients for the independent variables when not included in the model were significantly different from 0 which meant the addition of one more of the variables affects the predictive power of the model (Field, 2005). Based on the goodness-of-fit, the analysis proceeded to test the significance of each independent variable.

Test of individual variables for models

Significant relationships between sleep and the individual predictors were based on odds ratios with a 95% confidence interval outside of 1.0 and $p\leq0.05$ (Tabachnick & Fidell, 2001). Results showed that when group was entered into the logistic regression model, significant predictors of poor sleep included being a BCS having hot flashes, poor

physical functioning, depressive symptoms, and impact of a life event (see Table 14). Results were evaluated on the basis that odds ratios greater than 1 related to increased odds for poor sleep. After adjusting for all other predictors, the poorest sleepers were women who were BCS (OR=1.70), had hot flashes (OR=2.32), had poor physical functioning (OR=3.02), had depressive symptoms (OR=4.17), or had moderate (OR=2.92) or high levels of distress related to a life event (OR=4.09 to 5.70).

Table 14

Summary of Model 1: Logistic Regression Analysis Predicting Poor Sleep

Predictor	β	SE	Odds ratio	Wald statistic	95% CI	
					Lower	Upper
Group (BCS) [1]	0.53	0.22	1.70	5.69*	1.10	2.63
Race (Minority)[2]	0.46	0.27	0.05	0.03	0.61	1.78
Post-menopausal[3]	0.70	0.27	0.05	2.07	0.63	1.81
Low income[4]	0.20	0.23	1.21	0.69	0.77	1.92
2 or more co-morbidities[5]	0.43	0.47	1.54	0.83	0.61	3.91
Hot flashes[6]	0.84	0.22	2.32	14.57*	1.50	3.58
Poor physical functioning[7]	1.10	0.26	3.02	17.20*	1.51	5.08
High depressive symptoms[8]	1.43	0.33	4.67	19.34*	2.21	7.87
High impact of life event						
Mean score=1-2	1.07	0.45	2.92	5.70*	1.21	7.04
Mean score=3 or more	1.44	0.53	4.2	4.09*	1.48	11.99
Having bed partner[9]	0.01	0.27	1.01	0.00	0.60	1.70
Children in the home[10]	-0.02	0.23	0.98	0.01	0.63	1.53

*p≤0.05, 1=Referent WWBC, 2=Referent Caucasian, 3=Referent pre-menopausal, 4=Referent income over $50,000/yr, 5=Referent 1 comorbidity or less, 6=no hot flashes, 7=PF-10 scores 26-30, 8=Referent no depressive symptoms, 9=Referent no bed partner, 10=Referent no children in the home

The second regression model evaluated the predictors of poor sleep in BCS (see Table 15).

Table 15

Summary of Model 2: Logistic Regression Predicting Poor Sleep for BCS

Predictor	β	SE	OR	Wald statistic	95% CI	
					Lower	Upper
Race (Minority) [1]	1.14	0.47	3.14	5.99*	1.26	7.83
Post-menopausal[2]	0.52	0.35	1.67	2.15	0.84	3.33
Low income[3]	0.40	0.39	1.49	1.08	0.70	3.20
2 or more co-morbidities[4]	-0.09	0.83	0.91	0.01	0.18	4.69
Hot flashes[5]	0.99	0.33	2.68	9.10*	1.41	5.00
Poor physical functioning[6]	0.94	0.42	2.57	4.99*	1.12	5.86
Effects of cancer**						
# symptoms=0-5	0.36	0.43	1.43	0.69	0.61	3.33
# symptoms=6 and above	0.26	0.47	1.30	0.32	0.52	3.26
High depressive symptoms[7]	1.53	0.45	4.62	11.50*	1.91	11.78
High impact of a life event						
Mean score=1-2						
Mean score=3 or more	0.72	0.70	2.06	1.06	0.52	8.11
	1.02	0.90	2.77	1.29	0.48	16.10
Having bed partner[8]	0.45	0.41	1.56	1.21	0.70	3.46
Children in the home[9]	-0.53	0.32	0.59	2.71	0.32	1.11

*p≤0.05, **BCS only, 1=Referent Caucasian, 2=Referent pre-menopausal, 3=Referent income over $50,000/yr, 4=Referent 1 comorbidity or less, 5=no hot flashes, 6=PF-10 scores 26-30, 7=Referent no depressive symptoms, 8=Referent no bed partner, 9=Referent no children in the home

After adjusting for all other predictors, the poorest sleepers among BCS were minorities (OR=3.14), those with hot flashes (OR=2.68), those with poor physical

functioning (OR=2.57), and those with depressive symptoms (OR=4.62) ($p \leq 0.05$). Long term cancer treatment effects (symptoms) did not significantly add to the model.

The third regression model evaluated the predictors of poor sleep only in the WWBC. Results shown in Table 16 suggest WWBC with hot flashes, low levels of physical functioning, or high depressive symptoms significantly predicted poor sleep. Significant relationships between sleep and the individual variables were based on odds ratios with a 95% confidence interval outside of 1.0 and $p \leq 0.05$ (Tabachnick & Fidell, 2001).

Table 16

Summary of Model 3: Logistic Regression Predicting Poor Sleep for WWBC

Predictor	β	SE	OR	Wald statistic	95% CI	
					Lower	Upper
Race (Minority)[1]	-0.70	0.39	0.50	3.26	0.23	1.06
Post-menopausal[2]	-0.24	0.35	0.79	0.46	0.40	1.57
Low income[3]	-0.32	0.41	0.72	0.63	0.33	1.61
2 or more co-morbidities[4]	0.82	0.64	2.27	1.66	0.65	7.89
Hot flashes[5]	0.78	0.32	2.18*	5.89	1.16	4.09
Poor physical functioning[6]	1.29	0.38	3.61*	11.55	1.72	7.58
High depressive symptoms[7]	1.93	0.52	6.92*	13.69	2.48	19.28
High impact of a life event						
Mean score=1-2	1.01	0.65	2.74	2.42	0.77	9.74
Mean score=3 or more	1.38	0.73	3.99	3.52	0.93	3.68
Having bed partner[8]	-0.34	0.39	0.71	0.76	0.33	1.53
Children in the home[9]	0.61	0.35	1.85	3.04	0.93	3.68

*$p \leq 0.05$, 1=Referent Caucasian, 2=Referent pre-menopausal, 3=Referent income over $50,000/yr, 4=Referent 1 comorbidity or less, 5=no hot flashes, 6=PF-10 scores 26-30, 7=Referent no depressive symptoms, 8=Referent no bed partner, 9=Referent no children in the home

After adjusting for all other variables the poorest sleepers in the WWBC group were women with hot flashes (OR=2.18), poor physical functioning (OR=2.18), and depressive symptoms (OR=6.92) ($p \leq 0.05$)

Interpretation of residuals

Finally, the residuals of the logistic regression models were examined through frequency analysis for possible cases that poorly fit each model and cases that exert

unwarranted influence on the model through Studentized residuals, standardized residuals and deviance statistics (Field, 2005; Tabachnick & Fidell, 2001). Cook's distance, DFBeta, and leverage statistics revealed no values greater than 1 for any of the models suggesting no influential cases were found that negatively impacted the regression model (Field, 2005; Tabachnick & Fidell, 2001).

In summary, research question 3 evaluated predictors of poor sleep. Chi-square tests of independence showed variables significantly associated with a dichotomous sleep variable, which were then entered into the logistic regression models. Results showed that BCS status, hot flashes, physical functioning, depressive symptoms, and distress related to a life event predicted the presence of poor sleep when group was included in the regression. Specific predictors for BCS included minority status, hot flashes, physical functioning, and depressive symptoms. Specific predictors for WWBC included hot flashes, poor physical functioning, and high depressive symptoms.

Research question 4

To answer research question 4, "What are the physiological, psychological, and environmental predictors of the severity of sleep-wake disturbances (defined by PSQI global scores) of BCS and age-matched WWBC?", multiple regression was performed using three steps: (1) evaluate relationships between sleep and predictors; (2) examine multiple regression assumptions; and (3) perform multiple regression.

Step 1: Relationships between independent variables and sleep

Relationships between global sleep scores and continuous variables were evaluated using Pearson correlations shown in Table 17. Relationships were considered significant if the p-value was $p \leq 0.25$. These variables were then entered into the

regression model. As with research question 3, using a liberal p-value allowed for marginal relationships to be evaluated. Results showed that number of non-cancer related co-morbid conditions was correlated with global sleep scores. In addition, sleep was highly correlated with physical functioning, depressive symptoms, long-term effects of cancer, and impact of a life event. There was a weak correlation with concerns about recurrence and no correlation with age.

Table 17

Pearson Correlations Between Sleep and Continuous Predictors

		Age	Co-morbid	PF-10	CES-D	CARS[1]	SER total[1]	IES
PSQI	r	0.02	0.35*	-0.37*	0.47*	0.15*	0.37*	0.27*

1=BCS only, 2=non-cancer related co-morbid conditions, *p≤0.25

The remaining categorical predictors were evaluated using t-tests and analysis of variance (ANOVA) with post-hoc Scheffe tests (Field, 2005; Tabachnick & Fidell, 2001). Results showed that BCS had higher global sleep scores compared to WWBC t=4.62 (490), p≤0.01). For education, women with a high school education or less did not have significantly higher global sleep scores compared to women with college or grad school education F(2, 489)=1.44. In terms of race, minority women had higher sleep scores t=-.43 (490), p≤0.01 compared to Caucasian women. Socioeconomic predictors included income and work status. Those with higher income had lower global scores compared to lower income women F(7, 484)=19.00, p≤0.01). Women working full or part-time did not have significantly different sleep scores compared to unemployed women t=0.02 (490). For menopausal status, women who were post-menopausal had significantly higher global sleep scores t=-4.81 (490), p≤0.01 than pre-menopausal women. Women with hot

flashes had significantly higher sleep scores t=-6.42 (490), p≤0.01. Lastly, women with a bed partner t=3.13 (490), p≤0.01 and women with children living in the home t=-2.05 (490), p≤0.05 had significantly higher sleep scores. Variables were entered into the multiple regression model with a significance level of p≤0.25.

Breast cancer-specific categorical predictors included type of treatment and use of hormone modulators. Results showed that those not currently taking a hormone modulator had significantly higher global sleep scores F(2, 244)=5.37, p≤0.01 than women who were taking hormone modulators. Type of cancer treatment was not related to high sleep scores (t=1.88 (244), p=0.70) and not included in the regression model.

Relationships among the predictors are shown in Table 18. Bivariate correlations (Pearson r) were performed for continuous variables and dichotomous variables (Field, 2005). Chi-square tests of independence were performed for the categorical predictors with three or more groups.

Table 18

Test of Association Among Predictors

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Age	S	S	S	S	NS	.02	.31*	.50*	.07	-.33*	.02	.03	-.24*	-.04	S	S
2. Race		S	S	S	S	S	S	S	S	NS	S	NS	S	S	S	S
3. Education			NS	S	NS	NS	S	NS	S	NS	NS	S	S	S	NS	S
4. Work status				NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	S	S
5. Income					S	S	S	S	S	S	NS	S	NS	S	S	S
6. Sleep						.33*	S	.31*	S	-.38*	.37*	.47*	.15*	.27*	S	S
7. Co-morbid							.27*	.08	NS	-.51*	.25*	.36*	.01	.14*	NS	S
8. Menopausal								.33*	S	-.27*	.13*	.15*	-.02	.03	S	S
9. Hot flashes									NS	-.10	.12	.13*	.10	.02	S	NS
10. BCS tx[1]										NS	NS	NS	NS	NS	S	S
11. PF-10											-.38*	-.40*	.04	-.15*	S	S
12. Cancer s/e[1]												.38*	.22*	.43*	NS	NS
13. CES-D													.31*	.48*	NS	S
14. CARS[1]														.51*	NS	NS
15. IES															NS	S
16. Children																NS
17. Bed partner																

*p<0.05, 1=BCS only, numeric values represent Pearson correlation coefficient, NS=non-significant chi-square, S=significant chi-square p<0.05

Step 2: Testing assumptions

The assumptions of regression were evaluated before and after the analysis to establish that assumptions of; (1) non-collinearity, (2) absence of outliers, (3) normality, linearity, homoscedasticity of residuals, and (4) independence of errors were not violated. The third and forth assumptions evaluated residuals of the regression models. This evaluation was performed after the regression models were completed and is discussed in step three.

First, multicollinearity and singularity were examined prior to the multiple regression analysis by group. This step established a list of predictors that had strong relationships and determined if two measures were evaluating the same predictor variable. Strong collinearity between measures creates a situation where variables are competing for variance which would make it difficult to determine the importance of the competing predictors (Field, 2005). Although results showed significant relationships among certain predictors for both BCS and WWBC, for the test of collinearity, Pearson correlation coefficients > |0.70| were considered significant and would require examination (Tabachnick & Fidell, 2001). Based on that cut-off, no questionnaires were considered to have collinearity that would pose a problem for the multiple regression models (Table 19).

Table 19

Pearson Correlations for Test of Multicollinearity

		1	2	3	4	5	6
1	PSQI global	---	-0.36*	0.48*	n/a	n/a	0.32*
2	PF-10	-0.37*	---	-0.44*	n/a	n/a	-0.11
3	CES-D	0.44*	-0.36*	---	n/a	n/a	0.50*
4	CARS[1]	0.15*	0.04	0.31*	---	n/a	n/a
5	SER[1]	0.37*	-0.38*	0.38*	0.21*	---	n/a
6	IES	0.30*	-0.23*	0.52*	0.53*	0.43*	---

Above diagonal =WWBC, below diagonal=BCS, *$p \leq 0.05$, * $p \leq 0.01$, n/a=not administered.

In addition, frequency distribution curves were examined to determine the presence of outliers for categorical and continuous independent and dependent variables. This was a necessary step to determine if transformations were necessary prior to the multiple regression equations in question 4. Based on histogram frequency distributions, three scales were identified to have minor skewness due to outliers, including the IES (positively skewed), CES-D (positively skewed), and PF-10 (negatively skewed). All other items or scores showed normal distribution curves. For these measures, it was determined that the amount of skewness (based on the equation [skewness/standard error]) was less than 2.5 for the IES, CES-D, and PF-10 which is considered allowable, thus, scores were not transformed prior to the regression (Morgan, 2007).

The first step of the regression analysis evaluated significant relationships among the continuous and categorical person characteristics, physiological, psychological, and environmental predictors. Multiple regression can be used with predictor variables that are correlated with each other and with the dependent variable to a degree (Tabachnick & Fidell, 2001). However, according to Tabachnick and Fidell, it is optimal to have

independent predictor variables that are strongly correlated with the dependent variable but not strongly related to the other independent variables being evaluated. Having uncorrelated independent variables makes the interpretation of each variable contribution to the regression model more clear-cut (Field, 2005; Tabachnick & Fidell, 2001). Relationships were examined using collinearity diagnostics as part of regression models.

Step 3: Regression models of predictors and sleep

The standard model approach of multiple regression was selected for the final analysis. Although this method is considered atheoretical because it enters all independent variables at once with no hypotheses, the use of the standard approach answered the exploratory question of relationships among variables and how they impact the severity of sleep (Tabachnick & Fidell, 2001). Relationships were considered significant for all comparisons if $p \leq 0.05$.

Three separate multiple regression models were performed based on significant relationships with global sleep scores. The first model evaluated all predictors applicable to both BCS and WWBC after preliminary examination of variables. The second model evaluated predictors and cancer specific variables for BCS only. The third model evaluated predictors for WWBC only.

Variables included in each model

To begin, significant predictor variables related to sleep ($p \leq 0.25$) were entered into all three multiple regression models; group (model 1 only), race, income, menopausal status, number of co-morbid conditions, hot flashes, mean PF-10 scores, mean CES-D scores, mean scores from IES using two-subscales, presence of a bed partner, and presence of children in the home. For specific predictors of sleep-wake

disturbances in BCS, multiple regression procedures were repeated for the second model and included cancer specific variables. To determine specific predictors of sleep-wake disturbances in WWBC, multiple regression procedures were repeated for the third model. Field (2005) recommends entering all predictors in a standard entry regression then selecting the significant predictors and running a second regression model for interpretation. Based on the findings of the preliminary multiple regression model, a second and final model was executed and included only significant predictors of group, number of co-morbid conditions, hot flashes, PF-10 scores, CES-D scores, and IES scores. The final regression models showed the following significant relationships and are presented in Table 20.

Model 1 overall fit.

The interpretation of results included overall model summary and model parameters. First, the model summary for the final regression model showed that the predictors in the model accounted for 34% of the variability in the outcome ($R=0.58$, $R^2=0.34$). The ANOVA results showed that the model with the predictors was significantly different from the model without the predictors ($F=40.69$ (6, 485), $p\leq0.00$), thus, the model is a better predictor of poor sleep when the variables are included (Field, 2005) establishing goodness-of-fit.

Model 1 parameters.

The model parameters evaluated the unique contribution of each predictor variable in the regression model. Significant predictors of sleep included group, number of co-morbid conditions, hot flashes, level of physical functioning, depressive symptoms, and impact of a life event. The β values show that higher global sleep scores were

reported by women in the breast cancer group, women with a higher number of co-morbidities, those having hot flashes, lower levels of physical functioning, higher depressive symptoms, or reporting a greater impact of a life event (see Table 20).

The standardized beta value (β) provides information about the number of standard deviations that would change global sleep scores as a result of one standard deviation change of the predictor variable (Field, 2005). To interpret findings, the standard deviation of the global sleep score was multiplied by the final beta value for each significant predictor (β*SD). The result was interpreted as the number of points that the global sleep score would be projected to increase with one standard deviation change of the predictor. This would only be a valid if the other predictors were held constant (Field, 2005). This method of interpretation was used for all three models.

For model 1, the interpretation of results was based on the standard deviation of global sleep scores for the entire sample (SD=3.71). For group (β=0.11), since it is a dichotomous variable with no standard deviation, it was a challenge to interpret the unique contribution of the outcome. Therefore, it was projected that as more women were classified as BCS, global sleep scores would be projected to increase by 0.41 points (0.11*3.71). In terms of co-morbid conditions, as the number of co-morbid conditions increases by one standard deviation (SD=1.76), global sleep scores would increase by 0.11 standard deviations (β=0.11). Therefore, for each additional 1.76 co-morbid conditions, global sleep scores are projected to increase by 0.41 points (0.11*3.71). For every 1.57 increase in the number of hot flashes, global sleep scores are projected to increase by 0.74 points (0.20*3.71). For every 0.50 decrease in physical functioning scores, global sleep scores will increase by 0.63 points (-0.17*3.71). For every 9.48

increase in CES-D scores (depressive symptoms), global sleep scores are projected to increase by 1.04 points (0.28*3.71).

Model 2 overall fit.

The summary for the second regression model showed that the variables in the final BCS model accounted for 33% of the variability in the outcome ($R=0.57$, $R^2=0.33$). The ANOVA results showed that the final BCS model with the predictors was significantly different from the model without the predictors ($F=29.53$ (4,241), $p<0.00$), thus, the model is a better predictor of poor sleep when the variables are included (Field, 2005) establishing goodness-of-fit.

Model 2 parameters.

Significant predictors of sleep specific for BCS included number of co-morbid conditions, hot flashes, side effects of cancer, and depressive symptoms. The β-values showed that BCS with higher number of co-morbidities, reporting hot flashes, more long-term side effects from cancer, and higher depressive symptoms reported higher global sleep scores (poorer sleep quality and higher sleep disturbances) (see Table 20).

For model 2, the interpretation of results was based on the standard deviation of BCS global sleep scores (SD=3.80) multiplied by the final beta value for each significant predictor. For every 1.49 increase in the number of hot flashes, global sleep scores are projected to increase by 0.95 points (0.25*3.80). For every 3.62 increase in long-term effect of cancer, global sleep scores would increase 1.06 points (0.28*3.80). For every 9.60 increase in CES-D scores, global sleep scores are projected to increase by 0.68 points (0.18*3.80).

Model 3 overall fit.

The interpretation of results included overall model summary and model parameters. First, the model summary for the final regression model showed that the predictors in the WWBC model accounted for 31% of the variability in the outcome ($R=0.54$, $R^2=0.29$). The ANOVA results showed that the model with the predictors was significantly different from the model without the predictors ($F=19.92$ (10, 235), $p<0.00$), thus, the model is a better predictor of poor sleep when the variables are included (Field, 2005) establishing goodness-of-fit.

Model 3 parameters.

Significant predictors of sleep specific for WWBC included hot flashes, level of physical functioning, depressive symptoms, and impact of a life event. The B-values showed that WWBC reporting hot flashes, lower levels of physical functioning, higher depressive symptoms, or with distress related to a life event predicted higher global sleep scores (see Table 20).

For model 3, the interpretation of results was based on the standard deviation of WWBC global sleep scores (SD=3.45) multiplied by the final beta value for each significant predictor. For every 1.27 increase in the number of hot flashes, global sleep scores are projected to increase by 0.48 points (0.14*3.45). For every 0.49 decrease in physical functioning scores, global sleep scores would increase 0.59 points (0.17*3.45). For every 9.20 increase in CES-D scores, global sleep scores are projected to increase by 1.07 points (0.31*3.45). For every 1.39 increase in the impact of life event score, global sleep scores would increase 0.48 (0.14*3.45)

Table 20

Summary of Multiple Regression Results

	PSQI Global Both groups combined		PSQI Global BCS only		PSQI Global WWBC only	
	Prelim	Final	Prelim	Final	Prelim	Final
Variable	β	β	β	β	β	β
Group	0.11*	0.11*	----	----	----	----
Race	0.03	----	0.11	----	-0.09	----
Income	-0.01	----	-0.06	----	-0.05	----
Menopausal status	0.01	----	0.04	----	-0.01	----
Co-morbid conditions	0.11*	0.11*	0.13*	0.20*	0.05	----
Hormone modulator[1]	n/a	n/a	-0.07	----	----	----
Hot flashes	0.20*	0.20*	0.24*	0.25*	0.14*	0.14*
Physical functioning	-0.16*	-0.17*	-0.10	----	-0.15*	-0.17*
Long term effects of cancer[1]	----	----	0.14*	0.28*	----	----
Concerns about recurrence[1]	----	----	0.10	----	----	----
Depressive symptoms	0.28*	0.28*	0.23*	0.18*	0.20*	0.31*
Impact of life event	0.11*	0.11*	-0.02	----	0.14*	0.14*
Having bed partner	-0.10	----	0.01	----	-0.06	----
Children in the home	-0.02	----	-0.01	----	0.00	----
Model						
F	22.19	22.05	10.46	29.53	10.74	19.92
p	0.00	0.00	0.00	0.00	0.00	0.00
R^2	0.34	0.34	0.37	0.33	0.31	0.29

*$p \leq 0.05$, 1=BCS only

Checking of assumptions for all models

The last step of the data interpretation evaluated the assumptions of the regression equations. First, based on the tolerance and VIF scores, no variables approached 0 or exceeded 10 which would indicate concern of multicollinearity (Field, 2005; Tabachnick & Fidell, 2001). In addition, standardized and studentized residuals (differences between predicted and obtained dependent values) for linearity, homoscedasticity, normality, and independence of error were evaluated. Normality of the residuals for global sleep scores showed histograms with normal curve distribution verifying that the errors of the predictor were normally distributed around the predicted dependent scores (Tabachnick & Fidell, 2001). Linearity was verified by examination of plotted residuals on a scatter plot diagram that was rectangular in shape with a positive direction. Homoscedasticity was verified that standard deviations of errors for the predicted values were nearly the same for global sleep scores (Tabachnick & Fidell, 2001) through visual interpretation of the scatter plot that showed a band of residuals with equal width. Lastly, independence of error showed a Durbin-Watson statistic of 1.83 for model 1, 1.76 for model 2 and 1.93 for model 3. The three results were near 2.0 which is optimal to show that the errors of prediction are independent (Field, 2005; Tabachnick & Fidell, 2001). Based on this examination of residuals, no assumptions of the multiple regression models were violated.

In sum, the multiple regression models showed significant predictors of sleep quality when group was included in the equation were group membership, hot flashes, physical functioning, depressive symptoms, and impact of a life event. However, level of physical functioning and impact of a life event were non-significant in the BCS only

model. Significant predictors for WWBC include hot flashes, level of physical functioning, depressive symptoms, and impact of a life event. Finally, the assumptions of the regression models showed no violations that would negatively impact the results.

Summary

The purpose of this chapter was to determine the difference in prevalence, severity, and predictors of sleep-wake disturbances between BCS and WWBC. Four research questions were addressed and showed that BCS had greater prevalence and more severe sleep-wake disturbances compared to age-matched WWBC. Predictors of sleep-wake disturbances were evaluated between BCS and WWBC with cancer related variables of long-term effects of cancer also predicting sleep problems specific to BCS. Findings showed some similarity in predictors for prevalence and severity between BCS and WWBC (hot flashes, depression) but differences were also noted. The final chapter will discuss these findings in relation to current literature regarding sleep-wake disturbances in BCS. In addition, strengths and limitations will be addressed as well as implications for nursing practice and recommendations for future research.

CHAPTER FIVE

DISCUSSION

The purpose of this research study was to gain further knowledge regarding the prevalence, severity, and predictive factors of sleep-wake disturbances in BCS compared to age-matched WWBC. The secondary analysis of quantitative questionnaires provided data to answer the following research questions:

1. Is there a difference in the prevalence of sleep-wake disturbances between BCS and age-matched WWBC?
2. Is there a difference in the severity of sleep-wake disturbances (defined by PSQI global scores and 7 component scores) between BCS and age-matched WWBC?
3. What are the physiological, psychological, and environmental predictors of poor sleep (defined by PSQI scores >5) in BCS and age-matched WWBC?
4. What are the physiological, psychological, and environmental predictors of the severity of sleep-wake disturbances (defined by PSQI global scores) of BCS and age-matched WWBC?

The purpose of this chapter is to; (1) present research findings and relate findings to existing sleep-wake disturbance literature, (2) present strengths and limitations of the study, (3) describe implications for practice, and (4) provide recommendations for future research. A brief summary will close the chapter.

Research Findings

In this section, findings are discussed and related to results from current literature regarding sleep-wake disturbances in BCS. The following results are discussed below: (1)

sample characteristics, (2) prevalence and severity of sleep-wake disturbances, (3) predictors of prevalence and severity, and (4) revisions for the Elam Psychobiological Model. Recalling the gaps in the BCS sleep literature, the discussion will show how this study built upon previous findings by (a) including a comparison group, (b) using standardized conceptual and operational definitions of sleep-wake disturbances, (c) validating that sleep is a primary problem in long-term survivors, and (d) supporting the need for a unique psychobiological model of sleep-wake disturbances for BCS.

Sample characteristics

This section focuses on differences in sample characteristics including possible explanations for the findings. Differences in sample characteristics can be common when groups are not matched on certain criteria such as race, education, and menopausal status. Only one previous study of sleep disturbances compared BCS to a group of WWBC. In that study, no group differences were found after matching on age, race, and menopausal status (Carpenter et al., 2004). The current study found significant differences in race and menopausal status after matching for age. For race, even with the inclusion of a large set of minority women from the one parent study (AA study), there were more Caucasian women (73%) than minorities (27%) in this sample. These findings were reflected in previous BCS studies where racial categories ranged from 73-95% Caucasian (Carpenter & Andrykowski, 1999; Carpenter et al., 2004; Ganz, 2005). One possible explanation is the lack of long-term African American survivors (Northouse et al., 1999). African Americans with breast cancer tend to have more aggressive disease with lower survival rates (Jemal et al., 2008) reducing the number of subjects available for recruitment. In

addition, the geographical location or setting of the study could have reduced the number of minority women who were available for study recruitment.

As expected, this study contained more BCS (70%) than WWBC (53%). who were post-menopausal. When menopausal status was reported in BCS samples, previous findings were similar (Carpenter & Andrykowski, 1998, 1999; Carpenter et al., 2004). Even though this study included younger survivors that theoretically should be pre-menopausal, early menopause is a potential result of cancer treatment. BCS tend to experience premature ovarian failure, or early onset of menopause, as a result of breast cancer treatment such as surgery, chemotherapy, and use of hormone modulators (Crandall et al., 2004). This early menopause experience in younger BCS could be the reason for this large percentage of post-menopausal women.

Prevalence and severity of sleep-wake disturbances

The current study showed that sleep disturbances were more common and more severe among BCS (65%) than age-matched WWBC (55%). The prevalence rate for the problem in this study was within the range of prior BCS studies that included questions about sleep. These studies found that 19-90% of BCS complained of poor sleep or insomnia compared to 67% of WWBC (Carpenter & Andrykowski, 1999; Carpenter et al., 2004; Crandall et al., 2004; Davidson et al., 2002; Fortner et al., 2002; Northouse et al., 1999; Savard et al., 2001; Schultz et al., 2005). Three of these BCS studies had lower prevalence rates (19-49%), possibly because samples and sleep measures differed from this current study (Davidson et al., 2002; Northouse et al., 1999; Savard et al., 2001). These studies did not include comparison groups. One study of 98 African American BCS who were 4 years post-diagnosis used a single-item sleep question embedded in an

assessment of quality of life (Northouse et al., 1999). The other two studies used standardized questionnaires for specific types of sleep disturbance. Davidson et al. evaluated symptoms of insomnia, leg restlessness, and excessive sleepiness in a sample of 302 BCS (racial characteristics not reported) who were 2-5 years post-diagnosis. Savard et al. (2001) used a standardized measure of insomnia to evaluate sleep in 300 BCS who were 4 years post-diagnosis (racial characteristics not reported).

Three studies reported similar prevalence rates (61-67%) to the current study. These three prior studies used various measures and samples of BCS (Carpenter & Andrykowski, 1999; Crandall et al., 2004; Fortner et al., 2002). Fortner et al. (2002) used the PSQI to evaluate sleep in 72 breast cancer subjects that were mainly Caucasian and a mix of pre-treatment, in-treatment, and post-treatment women. This study included a comparison group but found no group differences in sleep variables. Carpenter & Andrykowski (1998) used a single-item question embedded in an assessment of menopausal symptoms in 114 BCS who were mainly Caucasian and a mean of 3 years post-diagnosis. Crandall et al. (2004) also used a single-item question for sleep in relation to menopausal symptoms in 476 BCS who were mostly Caucasian and 2-10 years post-diagnosis. It is interesting that these studies produced similar prevalence rates, despite differences in sample sizes, sample characteristics, and measures.

The studies with higher prevalence rates of 73% (Carpenter et al., 2004) and 90% (Schultz et al., 2005) used the PSQI or a single-item assessment of sleep in BCS. Carpenter & Andrykowski (1998) used the PSQI to evaluate sleep in 15 BCS who were mostly Caucasian and mean of 5 years post-diagnosis. This was the only study to report prevalence of sleep disturbances in a comparison group of WWBC. Schultz et al. (2005)

assessed sleep in relation to menopausal symptoms in 287 BCS. These women were mostly Caucasian and a mean of 16 years post-diagnosis. Although it was a study of menopausal symptoms, menopausal status of the women was not reported. Even with a varied sample size, both studies found higher prevalence of sleep complaints compared to this study.

In the current study, the severity of sleep disturbances (M=7.26 for BCS) was within the range reported in prior BCS studies (range=6.8-7.3) (Berger et al., 2003; Carpenter & Andrykowski, 1998; Carpenter et al., 2004; Fortner et al., 2002). The current study also found that WWBC had less severe sleep disturbances compared to two other comparison groups that reported means of 6.7 (n=50) (Fortner et al., 2002) and 6.9 (n=15) (Carpenter et al., 2004). In these studies and the current study, BCS had more severe sleep disturbances compared to WWBC.

In addition, this study suggests that long-term BCS are at greater risk of poor sleep and report more severe sleep disturbances compared to an age-matched group of WWBC. However, this comparison is only based on one previous study with a small sample size of women with hot flashes (Carpenter et al. 2004). The current study also showed that prevalence and severity of sleep disturbances in BCS is problematic in long-term survivors. In studies with similar findings, BCS were more than 2 years post-diagnosis suggesting that sleep disturbances are a problem for BCS after treatment and well into survivorship. These findings suggest that BCS are experiencing underlying problems that contribute to poor sleep and severe sleep disturbances such as depressive symptoms and menopausal symptoms such as hot flashes (discussed in detail below).

Predictors of poor sleep and severity of sleep disturbances

Current literature describing sleep disturbances in BCS used a variety of theoretical models to guide their research (e.g., Spielman's Three Factor Model) (Savard et al., 2001). Reflecting back to Chapter Two, no one model included physiological, psychological, and environmental predictors specific to BCS. This study was the first to examine a more comprehensive set of predictors specific to BCS. Findings from this study showed that predictors of poor sleep and severity of sleep disturbances in BCS were slightly different compared to age-matched WWBC. This information supports the need for a unique model with specific predictors that describe sleep-wake disturbances in BCS.

Revised models

Based on the significant predictors of poor sleep and sleep disturbances in BCS, the Elam Psychobiological Model could be revised as follows. Study findings suggested that minority BCS, with hot flashes, low levels of physical functioning, or depressive symptoms are at greatest risk for poor sleep. In addition, BCS with poor sleep tend to have more co-morbid conditions, hot flashes, long-term effects of cancer, or depressive symptoms. The revised models (see Figures 2 and 3) are based on these findings. Two models were produced to distinguish between prevalence and severity since predictors were slightly different for these two outcomes. Figure 2 targets predictors of poor sleep whereas Figure 3 targets severity of sleep disturbances. Both figures support the need for a psychobiological model since significant predictors were found in the person, physiological, and psychological categories. The models also provide visual depiction of which categories contain the majority of significant predictors. Figure 2 shows that

predictors are dispersed evenly for poor sleep whereas Figure 3 has more physiological predictors for severity. Even though the non-significant variables were tabled in the visual depiction of the revised models, it may be premature to remove the non-significant variables such as age, socioeconomic status, and sleep environment as these factors have been shown to contribute to poor sleep in previous studies. Even though some factors were not supported by this study, future studies with different sample characteristics or that include sleep hygiene factors could produce a different view of the model. In addition, asking women to answer questions in the context of sleep disturbances could also produce different results. Therefore, it is recommended to maintain these as possible predictors until other samples of BCS can be compared to WWBC to determine if the current findings can be replicated.

Figure 2: Revised Elam Psychobiological Model Prevalence of Poor Sleep

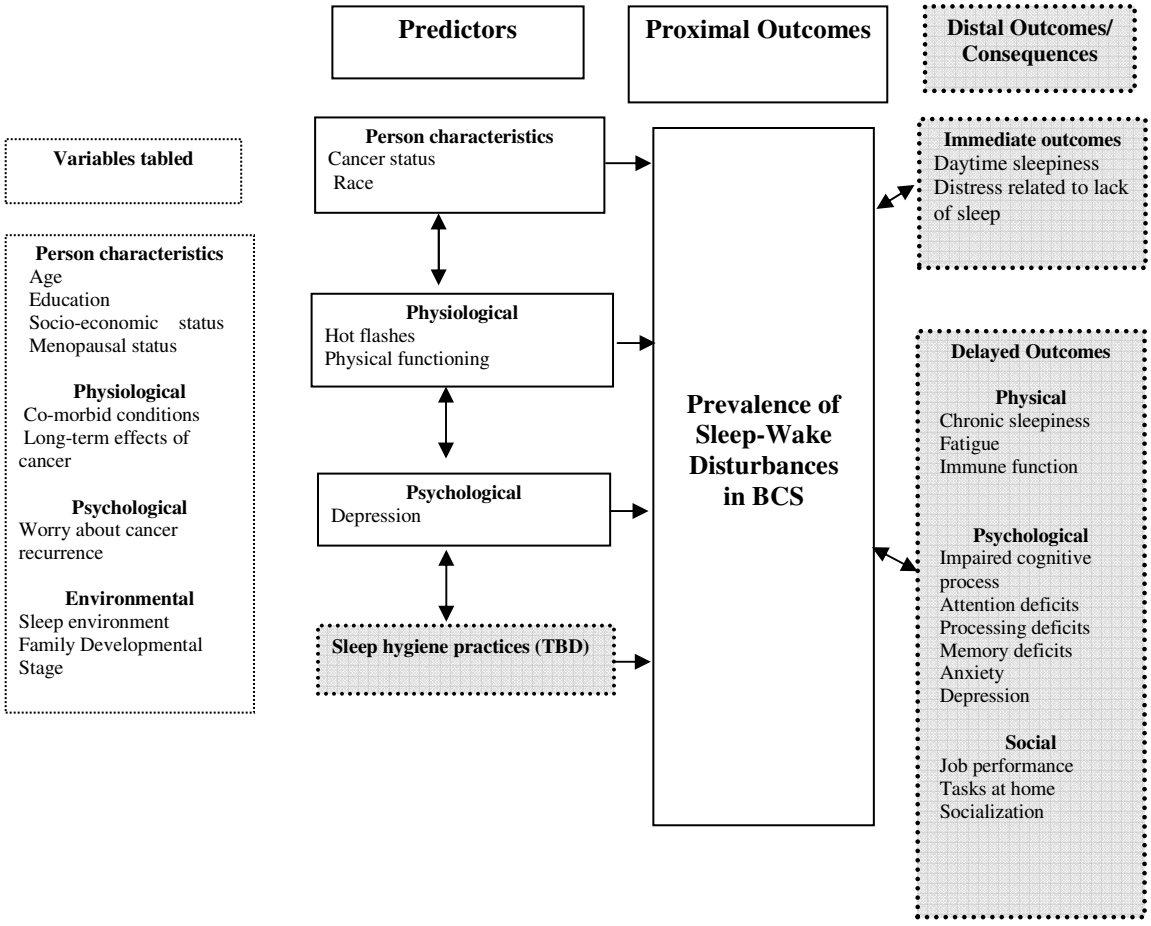
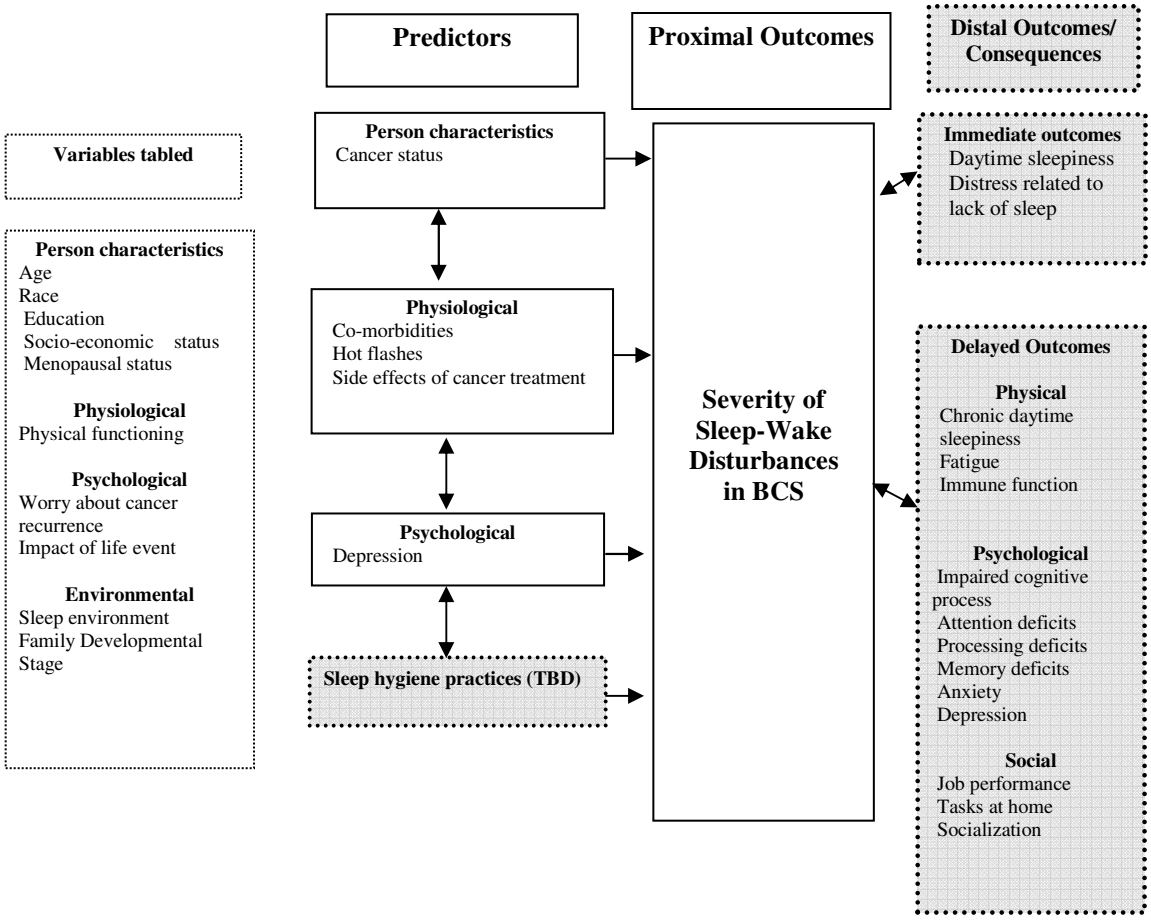


Figure 3: Revised Elam Psychobiological Model of Severity of Sleep-Wake Disturbances



The following sections addresses each variable evaluated and the resulting association with poor sleep and severity of sleep disturbances.

Person characteristics as predictors.

In addition to being female, person characteristics that impact sleep include; (a) having breast cancer, (b) race, (c) age, (d) socioeconomic factors, education, marital status, (e) menopausal status. Previous studies found that these factors (singly or in combination) can contribute to sleep-wake disturbances (Gellis et al., 2005; Hall, Bromberger, & Matthews, 1999; Hicks, Lucero-Gorman, Bautista, & Hicks, 1999;

Kravitz et al., 2003; Morin, Stone, Trinkle, Mercer, & Remsberg, 1993; Owens & Matthews, 1998; Polo-Kantola & Erkkola, 2004; Purves et al., 2004; Roehrs & Roth, 2004). Although this study found that being BCS and race were significant predictors of sleep disturbances, other variables were not significant. Each characteristic is discussed below.

As expected, having had breast cancer predicted both prevalence of poor sleep and severity of sleep disturbances. This supports a previous study that found BCS had poorer sleep and more severe sleep disturbances compared to WWBC (Carpenter et al., 2004). However, that study was not examining predictors of sleep but rather group differences in PSQI sleep variables. No other studies were found that included a comparison group in predicting sleep disturbances. The current study provides new information that being classified as a BCS is a risk factor for poor sleep and more severe sleep disturbances compared to WWBC.

An unexpected finding from this study was that minority BCS were at higher risk for poor sleep. Only one prior study evaluated sleep in African American (AA) BCS. The study focused on quality of life outcomes but reported 49% of the AA women had sleep problems based on a single-item question (Northouse et al., 1999). However, no prior sleep studies in BCS looked at race as a predictor of sleep disturbances. The only comparable study that looked at risk factors did not report the racial characteristics of the sample (Savard et al., 2001). The current study provides important information that minority BCS could be considered at higher risk for sleep disturbances compared to both Caucasian BCS and WWBC.

Interestingly, although previous studies found that age contributes to sleep disturbances in non-cancer populations (Morin et al., 1993; Shaver et al., 1991; Shaver & Giblin, 1989; Shaver & Zenk, 2000), age was not evaluated as a predictor of prevalence or severity of poor sleep for BCS or WWBC. The age range for BCS and WWBC in this study was 27-80 years of age. Based on prior studies, it was expected that younger BCS and WWBC might sleep better compared to older BCS and WWBC. For severity of sleep disturbances, age was not correlated with sleep scores for BCS or WWBC ($r=0.02$) and thus was not evaluated in the multiple regression. However, age was related to sleep as a dichotomous variable (good vs. poor). When evaluated with other variables, age did not predict prevalence of poor sleep. Non-significant findings suggest that poor sleep was problematic across ages in both BCS and WWBC. In addition, chronologic age of this sample is not consistent with menopausal status. Since the majority of BCS (young and old) were post-menopausal, it could be that menopausal status or the symptoms related to menopause are more important than chronologic age in this population. For example, sleep in a 30 year old post-menopausal BCS with hot flashes may not be the same as in a 30 year old BCS who is still pre-menopausal. It may be important in future studies to match samples on menopausal status.

This study did not support previous findings that socioeconomic factors, education, or marital status influence sleep. One prior study found that missed work time (OR=14.1), unemployment (OR=3.8), university education (OR=4.0), and widowhood (OR=4.7) were risk factors for symptoms of insomnia in BCS (Savard et al., 2001). Although missed work time was not evaluated as a predictor in this study, employment status, income, educational status, and marital status were not factors in predicting poor

sleep or severity of sleep disturbances in BCS or WWBC. One possible explanation for the difference is that Savard et al. focused on symptoms of insomnia, a specific type of sleep-wake disturbance instead of a general complaint of sleep disturbances.

Finally, this study also showed that menopausal status was not a predictor of poor sleep or severe sleep-wake disturbances in multivariate analyses. This was an interesting finding since univariate analyses indicated that menopausal status was related to poor sleep and sleep disturbances independently. There were no prior studies that looked at menopausal status as a predictor of sleep disturbances. However, prior studies showed that post-menopausal BCS with menopausal symptoms report sleep disturbances (Carpenter & Andrykowski, 1999; Carpenter et al., 2004; Schultz et al., 2005). This suggests that menopausal symptoms, rather than menopausal status, may be the most important factors in predicting prevalence and severity of sleep disturbances.

Physiological predictors.

No previous studies in BCS have evaluated physiological predictors of poor sleep. This study provided new information regarding physiological predictors such as; (a) presence of co-morbid conditions, (b) hot flashes, (c) levels of physical functioning, (d) presence of long-term side effects of cancer (e.g., lymphedema), and (e) breast cancer treatments.

There are a number of co-morbid conditions and their respective treatments that can negatively impact sleep. No prior studies were found that examined non-cancer medical conditions in relation to sleep-wake disturbances in BCS. Also, a comparison of the type of co-morbid conditions in BCS compared to WWBC was not found. This study provided new information regarding these two gaps. First, the mean number of co-morbid

conditions was the same for BCS and WWBC (M=2.0). However, the three most common types of co-morbid were slightly different between BCS and WWBC. The three most common co-morbidities in BCS were; first psychological disorders (depression, anxiety) (29%), second 'other' diseases not specified (18%), and third circulatory disorders (hypertension, hyperlipidemia) (19%), whereas, WWBC were; first circulatory disorders (19%), second psychological disorders (18%), and third 'other' diseases not specified (14%). These findings show that although the number of co-morbid conditions was similar, the types of co-morbid conditions for BCS are slightly different than WWBC. This information is useful since both depression and circulatory conditions can impact sleep (Savard & Morin, 2001).

Second, findings showed that the presence of co-morbid conditions (yes/no) did not predict poor sleep. However, the number of co-morbid conditions predicted severity of sleep disturbances in BCS and WWBC. This suggests that greater numbers of co-morbid conditions contribute to greater severity of sleep disturbances. This could mean that the side effects or treatments for these co-morbid conditions contribute to more sleep disturbances. Unfortunately, it is unknown whether the negative effects or treatments for these conditions were the underlying problem since this information was not available. Previous studies suggest that medications for co-morbid conditions, such as psychotropic and anti-hypertensive drugs, can negatively impact sleep (Bowman & Moshenin, 2003). It could be that side effects of these drugs were problematic for both BCS and WWBC in this study. Although findings were not unique to BCS, information that BCS with psychological and circulatory co-morbid conditions are at risk for greater severity of sleep disturbances is interesting. Future studies are needed to determine the impact of

these conditions (or the corresponding treatments) to the occurrence and severity of sleep disturbances in BCS.

It has been established that BCS who experience hot flashes report poor sleep (Carpenter et al., 2002; Savard, Davidson et al., 2004). Although this was not a unique factor for BCS, it has been reported that BCS tend to have more severe and distressing hot flashes when compared to WWBC (Carpenter, 2000; Carpenter et al., 1998). Hot flashes can be related to the use of hormone modulators which are used in breast cancer treatment. Interestingly, the majority of BCS in this study were not taking hormone modulators (67%). These findings suggest that BCS with poor sleep have hot flashes that were not caused by hormone modulators. This suggests that hot flashes are a physiological problem that should be examined when assessing complaints of sleep-wake disturbances in BCS.

The level of physical activity has been shown to decrease during breast cancer treatment contributing to sleep disturbances (Berger, 1998; Berger & Farr, 1999). It is unclear whether the decrease in activity during treatment continues into survivorship. It is unclear if physical functioning contributes to this lowered activity in BCS. Physical functioning, the ability to perform routine daily activities such as lifting groceries or climbing stairs, could be a factor in lowered activity. No prior studies have looked at the relationship between physical functioning and sleep disturbances in long-term BCS. For this study, low levels of physical functioning (limitations in daily function) predicted poor sleep in BCS and WWBC. However, physical functioning did not predict severity of sleep disturbances BCS. This suggests both BCS and WWBC with low levels of physical functioning are at risk of having sleep disturbances. This was an unexpected finding that

suggests low physical functioning or performance leads to prevalence of sleep disturbances. Although this finding was not specific to BCS, it suggests that future sleep research should examine physical functioning as a possible predictor of poor sleep. Determining the reason for the lowered functioning (e.g., arthritic pain) could provide information to facilitate effective interventions that improve sleep.

Although most side effects related to cancer treatment typically subside over time, some BCS experience residual effects that negatively impact quality of life (Dow et al., 2004). Such side effects include lymphedema, peripheral neuropathy, and chronic breast pain (Dow et al., 1996; Ganz, 2005; Ganz et al., 2002). No prior studies have determined if long-term effects of cancer are related to sleep-wake disturbances. For this study, long-term effects of cancer did not predict the presence of poor sleep. However, higher numbers of long-term effects predicted severity of sleep disturbances. This suggests that BCS with these symptoms are at greater risk for having more severe sleep disturbances. Although the symptom list was somewhat limited, this is an important finding since it identified a factor specific to BCS. In addition, this suggests that a complete assessment of cancer related symptoms is warranted since the reduction of such side effects can potentially reduce the severity of sleep disturbances.

Breast cancer treatment factors (chemotherapy, surgery, use of hormone modulators) did not predict poor sleep or severity of sleep disturbances. This an unexpected finding and contradicts previous findings from Savard et al. (2001) that found surgery (OR=5.2), chemotherapy (OR=4.3), and cancer stage (OR=0.46) predicted symptoms of insomnia. Radiation therapy was a constant for all subjects in that study and was not evaluated in the current study due to lack of data. Almost all subjects in the

current study received surgery and chemotherapy. This lack of sample variability could explain the lack of significant findings. In addition, the majority of BCS were not taking hormone modulators such as tamoxifen since they were more than 5 years post-diagnosis. Hormone modulators are designed to reduce estrogen in order to decrease breast cancer recurrence in hormone positive tumors. Decreased estrogen has been shown to increase sleep latency (Schiff et al., 1980). This suggests that the absence of estrogen itself can lead to sleep disturbances. However, it is unclear if other side effects of low estrogen, such as hot flashes, are the underlying reason for this disturbance.

Psychological predictors.

It has been well documented that psychological factors such as depression and anxiety are related to increased sleep disturbances (Anderson et al., 2003; Baker, Simpson, & Dawson, 1997; Carpenter et al., 2004; Miller, 2004; O'Connell, 2005; Okuyama et al., 2000; Roscoe et al., 2002). However, it is unclear if such disorders are predictors or consequences of sleep disturbances. For this study, these factors were considered predictors. Psychological factors evaluated included (a) cancer related distress (concerns of recurrence), (b) depression, and (c) distress related to a life event (non-cancer). First, distress related to concerns of breast cancer recurrence are problematic during survivorship (Cappiello, Cunningham, Knobf, & Erdos, 2007; Ferrell et al., 1996; Vickberg, 2003). It was thought that this concern could be related to general distress which is a common factor in sleep disturbances (Deimling et al., 2002). However, no previous BCS studies have linked this concern to sleep-wake disturbances. Results showed that although concern of recurrence was related to global sleep scores, it did not predict poor sleep or severity of sleep disturbances in BCS. This was an unexpected

finding since scores indicated that the BCS had moderate concerns regarding the recurrence of cancer (M=12.15, SD=5.51). Scores were also highly related to sleep when evaluated as an independent predictor suggesting it was important to include in the regression. This suggests that although BCS had concerns of recurrence, this concern did not contribute to sleep-wake disturbances. It could be attributed to other psychological problems such as depressive symptoms discussed below.

Second, depression is highly related to sleep-wake disturbances both in cancer and non-cancer populations (Baker et al., 1997; Carpenter et al., 2004; Clark et al., 1995; Deimling et al., 2002; Fava, 2004; Kloss, Tweedy, & Gilrain, 2004; Thase, 2005). Descriptive studies show that BCS report moderate to high levels of depressive symptoms during survivorship (Couzi et al., 1995; Dow et al., 1996; Ganz, 2005; Ganz et al., 2002; Northouse et al., 1999). One prior study looked at the combined effect of sleep, fatigue, and depressive symptoms in BCS compared to WWBC. Results showed that depressive symptoms were related to poor sleep in BCS (Carpenter et al., 2004). However, this was a small sample where the WWBC were more depressed than the BCS and did not evaluate predictive factors of the sleep. No prior BCS studies have looked at depression as a predictor of sleep-wake disturbances. This study provided new information that moderate levels of depressive symptoms were related to poor sleep and severity of sleep disturbances in BCS. In addition, higher levels of depressive symptoms were associated with more severe sleep disturbances in BCS and WWBC. This suggests that long-term survivors have high depressive symptoms that should be addressed and which are an important factor in poor sleep and sleep disturbances. Future studies will

need to distinguish whether depression is better modeled as a predictor or an outcome of poor sleep.

Lastly, BCS can experience distress related to the diagnosis of cancer (Bleiker et al., 2000; Cappiello et al., 2007; Dow et al., 1996; Tatrow, Montgomery, Avellino, & Bovbjerg, 2004). Only one study found that BCS reported high levels of distress related to cancer and poor sleep (Dow et al., 1996). No other BCS study looked at distress as a predictor of poor sleep or severity of sleep disturbances. The current study provides new information that distress related to breast cancer was not associated with poor sleep or severity of sleep disturbances. However, distress related to life event in WWBC was related to prevalence and severity of sleep disturbances. This can be attributed to the higher distress ratings by WWBC and that they answered questions based on any stressful life event that was not likely to be a cancer diagnosis. These were unexpected since the breast cancer experience has been found to be distressing and the Impact of Life Events scores were moderate for both intrusion and avoidance. These scores were also related to sleep independently. Since depression symptoms were high in BCS, it could be that depression and not distress experienced by long-term survivors contributes to poor sleep and/or sleep disturbances. Unfortunately, it is unclear if distress related to a non-cancer life event in BCS contributes to poor sleep and this requires further investigation.

Environmental predictors.

Sleep environment such as excessive light, noise, presence of a restless sleep partner, and child rearing have been shown to negatively impact sleep (Cheek et al., 2004; Dogan et al., 2005; Gentili, Weiner, Kuchibhatil, & Edinger, 1997; Shinkoda et al., 1998). Prior studies typically focus on inpatient hospital or nursing home settings where

excessive activity is routine (Dogan et al., 2005; Gentili et al., 1997). In addition, child rearing has been found to disrupt sleep due to frequent nighttime awakenings by a newborn or child (Miller, 2004). Although most BCS are at an age where children are no longer living at home, this study found a majority of women had children at home. Having a companion or bed partner with disrupted sleep can also contribute to the woman's own disrupted sleep (Fry, 1987; Jefferson et al., 2005; O'Donnell, 2004). No prior BCS studies evaluated if such factors contribute to poor sleep and sleep disturbances.

Two environmental factors were evaluated in this study; (a) having a bed partner and (b) having children in the home. Results showed that having a bed partner and children living in the home (child rearing) were not associated with poor sleep or sleep disturbances in BCS or WWBC. However, environmental factors included in the analyses were limited to one item questions and did not include factors such as noise, light, and sleep habits of the bed partner (restless sleeper). Since these other factors were not assessed, it is unclear whether these factors contribute to poor sleep and sleep severity in BCS. It could also be that these factors are not problematic and do not need to be assessed in BCS with poor sleep.

In summary, findings from this study were compared to previous research regarding sleep disturbances in BCS. These comparisons showed similarities and differences adding new knowledge to the literature and conceptualization of sleep disturbances in BCS. Overall, the results from this study suggest that there are unique factors associated with sleep-wake disturbances in BCS.

Strengths and Limitations

Strengths of this study included; (1) lack of missing data, (2) use of a large sample size of long-term survivors, (3) use of a standardized measure of sleep, and (4) assessment of a comprehensive set of variables. Each strength is discussed below.

First, a major strength was the lack of missing data in the parent datasets which can be a pitfall when conducting a secondary data analysis (Polit & Hungler, 1999). Missing items were randomly dispersed and less than 1% of the entire combined dataset. This reduced the number of subjects and/or cases that required deletion from the analyses.

A second strength was the large sample of long-term survivors and age-matched WWBC from the parent datasets. The current study sample was 16 times larger than one previous study reviewed (Carpenter et al., 2004). Study findings validated that women with BCS have more severe sleep problems compared to age-matched WWBC. This supports the notion that having breast cancer alone puts women at risk for greater sleep problems. In addition, having a sample of long-term survivors validated that sleep is a problem in BCS more than 5 years from diagnosis suggesting that sleep problems may persist over time.

Third, the study used the Pittsburgh Sleep Quality Index (PSQI) which is a validated measure of sleep disturbances in BCS. This facilitated comparisons with previous data adding to existing knowledge regarding the reliability of the PSQI in other samples of BCS and WWBC. Using the PSQI also provided standardized terminology to describe poor sleep and sleep disturbances based on the established cut-off for global sleep scores.

Finally, the comprehensive nature of the parent datasets provided a large number of variables to be evaluated. No previous studies have looked at a set of predictors in this manner. These results provided new information regarding predictors of sleep-wake disturbances specific to BCS. In addition, this study provided new knowledge that predictors of prevalence and severity are different for BCS suggesting the need for two separate conceptual models. This improves upon prior research in the conceptualization of sleep-wake disturbances in BCS.

There were also several limitations to this study. Limitations included; (1) matching only on age, (2) use of secondary data, (3) measurement issues and, (4) statistical issues. Each limitation is discussed below.

First, the sample was matched only on age and significant differences in race and menopausal status were found. In addition, because this was a convenience sample, the subjects may not have been representative of all BCS with and without sleep disturbances. Using a convenience sample has the potential for response bias by subjects that strive to convey either a positive or negative outlook of quality of life, thus, all responses are positive or negative (Polit & Hungler, 1999). For example, the sample included in this study could have been negative responders, thus, inflating the prevalence and severity of sleep disturbances for both BCS and WWBC. Because of this limitation, the results may not be representative of the greater population of BCS. However, this is unlikely due to the large sample size included in this study.

Next, the use of secondary data for this analysis had several limitations. First, several suggested variables could not be evaluated such as sleep hygiene behaviors, detailed sleep environment factors, and detailed breast cancer treatment information.

Findings showed 34% of the variance for sleep severity was explained by the variables evaluated. This leaves a moderate amount of unexplained variance in terms of severity of sleep disturbances. Factors such as thyroid function, genetic polymorphisms, sleep hygiene, and additional sleep environment factors could have been some of the missing pieces needed to increase the percentage of explained variance. Second, answers to questionnaires were completed from a quality of life perspective. Responses may have been different, such as higher global sleep scores, if subjects were completing questionnaires that focused solely on sleep disturbances.

Third, limitations included measurement issues. The reliability of the PSQI for both BCS and WWBC was near the cut-off for adequate reliability and lower than reported in a previous study that reported alphas of 0.80 for BCS and 0.83 in a non-cancer cancer population (Carpenter & Andrykowski, 1998). This lower reliability suggests that the items in the PSQI may not have captured the critical attributes of sleep disturbances for this sample. This could be attributed to the fact women did not understand the questionnaire, or, that the results reflected response burden since the parent studies included over 15 questionnaires. Women generally answered questionnaires in their home environment suggesting that distraction while completing the questionnaires could have led to misunderstanding. In addition, the lack of an objective measure of sleep limited knowledge regarding the type of sleep-wake disturbance experienced by BCS. It is not clear whether more BCS experience insomnia or some other type of physiological sleep disorder not captured by a subjective measure. This type of measurement is relevant since a recent study showed that physiological sleep

disorders, such as sleep apnea, are common in menopausal women (Freedman & Roehrs, 2007).

Lastly, statistical limitations are as follows. First, the use of standard entry can mask unique contributions of certain independent variables in the regression equation and appear unimportant to the model when actually there is some relationship present (Tabachnick & Fidell, 2001). Second, a generous alpha level (α=0.25) was used to evaluate significant relationships between sleep and the independent variables. Those with significant relationships were then entered into the regression models. By using a generous alpha there is higher probability that a Type II error was committed (accepting a false null hypothesis) (Polit & Hungler, 1999). Committing a Type II error means that the significant predictors reported from this study could in fact be insignificant. However, using a higher alpha was acceptable for this study since it was an exploratory analysis.

In addition, the term 'predictor' used to describe variables associated with sleep-wake disturbances could be misleading to readers. The term 'predictor' is typically used to make forecasts about how certain independent variables behave in a new setting with different populations (Polit & Hungler, 1999). The results provide support for the probabilistic estimate of future events based on those interactions. In research, regression using longitudinal designs, or data that has been collected over-time is used to evaluate predictor variables (Polit & Hungler, 1999). In the current study, the variables listed in the Elam Psychobiological Model were termed 'predictors' using a cross-sectional design. Some may argue that these variables should be labeled 'contributing factors' because the data was not evaluated over-time. However, recalling that factors associated with sleep disturbances can be precipitating (root cause) or perpetuating (cause over-

time), it would be difficult to determine which one is the source of the current sleep-wake disturbance. Therefore, the term 'predictor' was used to describe these relationships since the independent variable could be a perpetuating cause occurring over-time.

Implications for Practice

Nurses and other health care professionals play a vital role in the assessment of clinical issues among BCS. Nurses and other health care professionals who practice in all types of clinical settings (e.g., primary care, women's health) should be aware that BCS experience poor sleep and severe sleep disturbances. Since BCS are more at risk for having poor sleep and severe sleep disturbances, practitioners need to target BCS for enhanced screening of sleep-wake disturbances. Additionally, findings from this study suggest those at highest risk included BCS in the minority, having hot flashes, having than two co-morbid conditions, or with high depressive symptoms. BCS who are more then 5 years post-diagnosis tend to visit oncology clinics only once per year and return to primary care settings for acute health needs. This suggests that in long-term survivors, it is the primary-care practitioners that will be more likely to identify sleep problems in BCS.

Screening for sleep-wake disturbances can start with a simple one sentence question such as, 'How are you sleeping?' This could prompt a conversation regarding problems with sleep. Practitioners can then identify those BCS that would require more detailed assessments of sleep-wake disturbances. Including family members in this assessment is essential to gain additional information such as snoring or frequent limb movements during sleep. This could result in a referral to sleep specialists to rule out clinical sleep problems such as sleep apnea or restless leg syndrome. In addition, if a

clinical assessment reveals psychosocial or behavioral problems such as depression and poor sleep hygiene habits, referrals should be considered an important resource to determine the best intervention. Practitioners can perform initial teaching regarding sleep hygiene practices such as establishing a bed-time routine that includes avoiding eating 2 hours prior to bed, excessive activity prior to bed, or excessive caffeine intake. If patient education is completed, it is important to establish an appropriate follow-up to determine if further evaluation is needed.

Although negative consequences were not addressed in this study, general findings suggest that sleep-wake disturbances can lead to immediate and delayed physiological and psychosocial health related outcomes (Engstrom et al., 1999; Koopman et al., 2002; Moe, 2004; Northouse et al., 1999; Schultz et al., 2005). Problems such as daytime sleepiness, decreased immune function, and loss of job productivity could prompt BCS to seek health care intervention (Savard et al., 2003; Savard et al., 2001). Practitioners need to not only identify those with sleep problems but also evaluate negative outcomes associated with lack of sleep.

Since the number of women surviving breast cancer is projected to increase each year and BCS constitute the largest survivorship population (National Center for Chronic Disease Prevention and Health Promotion, 2004), sleep-wake disturbances will continue to be a clinical problem in need of intense evaluation by practitioners in both oncology and primary are settings. Addressing these issues from a clinical perspective can potentially decrease the negative outcomes related to sleep, thus, improving quality of life.

Future Research

Research findings from this study can guide future research. The following section outlines how these findings will; (1) guide measurement of poor sleep and sleep disturbances, (2) guide further conceptualization of sleep and sleep disturbances, and (3) guide development of targeted interventions of sleep-wake disturbances in BCS.

Findings showed that BCS reported poorer sleep and higher sleep disturbances compared to WWBC. Sleep was measured using the Pittsburgh Sleep Quality Index (PSQI). This measurement was successful in identifying poor sleep and sleep disturbances in BCS even with a suboptimal Cronbach's alpha coefficient. Using the standardized questionnaire facilitated comparison to prior BCS sleep studies. Future studies should continue to use the PSQI to provide consistency in data findings. Addition of objective measurement, such as polysomnography, will help identify those with physiological problems not captured in subjective measures. Additional objective measurement should include hot flash monitoring since this was a strong predictor of poor sleep and sleep disturbances in BCS. In addition, using both subjective and objective measures provides the opportunity to determine if these are correlated.

In terms of conceptualization of sleep in BCS, future research should focus on refining predictors of specific groups and formulating targeted interventions for BCS. Studies should be conducted in a clinical setting to ensure accuracy and understanding of completed questionnaires by subjects. Further describing predictors of sleep specific to race will refine knowledge regarding those BCS at risk. In addition, longitudinal studies are needed using structural equation modeling or path analysis to validate pathways of this model and determine if predictors are consistent over time. Further model testing will

need to evaluate the portions of the model that have not been fully investigated such as sleep hygiene factors, types of sleep-wake disturbances, and health related outcomes such as marital satisfaction and sexual relationships of couples. This information will provide additional support to the model and refine current knowledge.

Overall, the model provides a more comprehensive theoretical framework that is lacking in current studies. This information is needed to guide research designs and test interventions to help treat this problem. There has been a national response to this type of research in the cancer population. The importance of understanding sleep disturbances in cancer populations has been highlighted by national funding agencies such as the National Institute of Aging, National Heart, Lung, and Blood Institute, National Institute of Neurological Disorders and Stroke (www.nih.gov), and continues to be a research priority of the Oncology Nursing Society (www.ons.org).

Future research could include constructing tailored interventions for sleep disturbances specific for BCS. However, before these interventions can be tested, additional descriptive work is needed. There is a lack of knowledge about the type sleep-wake disturbance experienced by BCS. A pilot study should be conducted that evaluates BCS for the presence of various types of physiological sleep disturbances such as sleep apnea and restless leg syndrome. This is supported by one study that showed 43% of BCS experienced restlessness in the legs (Davidson et al., 2002). In a study of non-cancer women, a study also found that a higher than expected percentage of menopausal women who reported poor sleep had undiagnosed physiological sleep disorders (Freedman & Roehrs, 2007). This type of assessment would include 1 or 2 nights of polysomnography study in a sleep laboratory.

In addition, concurrent psychological and behavioral interviews would need to also be conducted to obtain information regarding other factors contributing to sleep disturbances and health-related outcomes specific to poor sleep would also be recommended. Based this pilot data, an algorithm of tailored interventions could then be established based on the common types of sleep disturbances encountered specific to BCS. During recruitment for any BCS sleep studies, efforts to recruit more minority BCS should be strongly considered since minority BCS had the poorest sleep. Eventually, translation of research outcomes into primary care and medical oncology settings will further prompt identification and treatment of this problem.

Summary

This secondary analysis evaluated data from 246 BCS and 246 WWBC to determine prevalence, severity, predictors of poor sleep, and predictors of severity of sleep-wake disturbances. A comprehensive list of variables was evaluated to determine what factors predicted the prevalence and severity of poor sleep and sleep disturbances. BCS were more at risk for having poor sleep and more severe sleep disturbances compared to age-matched WWBC. Predictors of poor sleep specific to BCS were race, hot flashes, level of physical functioning, and depressive symptoms. Additionally, co-morbidities and long-term effects of cancer predicted severity of sleep disturbances. Results of this study supported findings in the current literature showing that sleep disturbances are problematic in long-term survivors. Contrary to previous studies, this study did not find that age, concerns about recurrence, or sleep environmental factors were factors in predicting poor sleep and sleep disturbances.

This study provided new information regarding predictors of poor sleep and sleep disturbances for BCS. Results provide a basis for recommendations for practice and future research that examines sleep over time in BCS. Findings of this study suggest that understanding sleep disturbances in BCS is multifaceted. Further examination of the health-related outcomes will provide additional further conceptual knowledge and drive research to develop effective interventions. The goal will be to reduce the negative outcomes through such interventions and improve the quality of life of BCS.

APPENDIX A

Summary of Theoretical Models

Author	Critical Attributes
Borbely, et al. (1999). Domain-medicine	• Physiological model of sleep. • Homeostatic process (Process S) rises during waking and declines during sleep. • Process S interacts with circadian process (Process C). • Course of daytime vigilance accounted by interaction of Process S and C. • Process S is from physiological variable (EEG slow wave). • Circadian dynamics includes non-REM and REM interactions with the process S and C. • PSG used for evaluation (not explicit).
Harvey (2002) Domain-psychology	• Cognitive model of sleep. • Developed in order to explain characteristics between sporadic vs. chronic insomnia. • Insomniacs experience unpleasant intrusive thoughts, worry during pre-sleep. • During wake periods, prone to increased anxiety, worry, neuroticism, obsessionality, dysphoria, hypervigilance, tension. • Cognitive processes trap: increases absorption and anxiety regarding sleep problem. • Excessive negative tone cognitions: getting enough sleep and how lack of sleep impacts health and daytime functions. • Excessive worry/ruminations: triggers autonomic arousal/emotional distress which lead to anxious state. • Selective attention/monitoring: monitor of internal sleep-related threats (not getting enough sleep, and not coping/functioning during day. • Overestimates extent of the perceived deficit of sleep and daytime performance. • Ultimate deficit/disruptions in sleep-wake cycles. • The perceived deficit then becomes a real sleep deficit. • Model accounts for nighttime awakenings.
Spielman et al. (1987) Domain-psychology	• Psychobiological model of sleep. • Multidimensional model of chronic insomnia provided interactions between predisposing, precipitating, and perpetuating factors of insomnia. • Explains the evolution of insomnia and how individual differences cause initiation of disturbed sleep. • Heightened arousal states (wake up easily) prone to poor sleep. • Lack of sleep continues, perpetuating factors of frustration, agitation about inability to sleep contribute to further cognitive and physiological arousal = increased lack of sleep.

Author	Critical Attributes
	• Maladaptive strategies include increased time to fall asleep, anxiety about daytime performance, and progression of psychological disorders such as anxiety and depression.
Espie (2002) Domain-psychology	• Psychobiological model of sleep. • Sleep is a default state of humans that contains involuntary, harmonious interactions between homeostatic and circadian processes in association with self-perception of good sleep quality. • Allows for normal variability of day-to-day sleep patterns (plasticity) and cognitive ability to deal with this variability. Failure of automated sleep activation and maintenance through precipitating factors that lead to persistent, chronic inhibition and prevention of natural recovery of good sleep. • Addresses the automaticity and plasticity of sleep and how it is weakened by inhibitory feedback from one or more psychobiological processes.
Elam, (unpublished) Domain-nursing	• Psychobiological model of sleep. • Predictors of sleep are unique to BCS and include physiological, psychological, environmental, and behavioral (sleep hygiene) factors. • Predictors can occur singly or clustered within and among each category of factors. • Predictors contribute to the occurrences of sleep-wake disturbances. • Precipitating factors can then become perpetuating. • Sleep-wake is operationalized by both subjective and objective measures. • Consequences include both immediate and distal outcomes that negatively impact quality of life. • Immediate outcomes include further sleep-wake disturbances due to negative cognitions about sleep. • Distal outcomes can also contribute to additional disturbances over time.

APPENDIX B

Descriptive Literature Tables

Predictors and outcomes

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Ancoli-Israel et al., 2001)	Cancer patients (review)	Pain Cancer treatment (chemotherapy, radiotherapy)	Psychiatric disorders (e.g., depression, anxiety)		Main variable: fatigue in cancer patients but reported on sleep issues Review states sleep is a common problem in cancer patient. Unknown: the relationship between treatment, distress, and/or palliative medication side effects and sleep-wake problem. Unknown: role of circadian rhythm disruption due to cancer itself, treatment for cancer, and long-term manifestations of that disruption. True cause of sleep-wake problems not identified in cancer patients. Common complaints: sleep latency, duration, awakenings, daytime dysfunction, daytime sleepiness, poor sleep quality. Pre-treatment cancer showed increased insomnia due to distress.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Anderson et al., 2003)	n=354 cancer patients n=psychiatric patients n=290 non-patient volunteers	Treatment-induced abnormalities in cytokine levels			Compared severity of fatigue between groups. Fatigue does not significantly differ between non-patient and depressed patients. 62% cancer patients reported moderate-severe sleep disturbance. Sleep disturbance significant predictor to severe fatigue. Links sleep disturbances and fatigue.
(Andrykowski et al., 1998)	n=88 breast cancer (BC) n=88 age matched benign breast problems				Main variable: fatigue after cancer treatment. Correlated various subjective fatigue questionnaires to find predictors of fatigue. PSQI results: no group differences in subscales except BCS had decreased sleep quality.
(Anker et al., 1998)	N=26 postmenopausal BCS				Thyroid function. Non-sleep specific. Reviewed to provide support for thyroid issues in BC.
(Berger, 1998)	n=72 BCS				Patterns of fatigue/activity/rest during adjuvant BC tx. Fatigue negatively correlated with activity. Evaluates sleep via activity and rest cycle (actigraphy).
(Berger & Farr, 1999)	n=72 BC patients	Treatment (chemotherapy)			Main variable: fatigue and sleep.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
		Disrupted circadian cycles due to inactivity			Women less active had increased night awakenings reporting higher fatigue during treatment. Disrupted sleep at mid-treatment are at risk for chronic fatigue. Less activity correlated with increased naps and higher fatigue.
(Berger & Higginbotham, 2000)	n=14 BC patients	Disrupted circadian cycles due to inactivity	Symptom distress		Main variable: fatigue and sleep. Fluctuating patterns of decreased activity, disturbed sleep, mild-moderate symptom distress correlated with moderate fatigue. Patterns of sleep (total sleep, latency, WASO, efficiency) differed from healthy norms. Highest fatigue and symptom distress during treatment. Fatigue correlated with: increased symptom distress, lower activity, poor physical/social health status.
(Berger & Walker, 2001)	n=60 BC patients		Reaction to diagnosis of BC Distress reaction to diagnosis of BC		Fatigue model: sleep is outcome variable. Person antecedents correlated with activity change (sleep) causing fatigue.
(Berger et al., 2003)	n=21 BC patients		Psychological factors (non-specific)		Sleep hygiene intervention followed over time. Adherence remained high for follow-up. Sleep-wake patterns were comparable to standard norms except for duration of nighttime awakenings.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Bleiker et al., 2000)	n=170 BCS				Used Impact of events Scale (IES) to determine distress after diagnosis of BC at baseline (prior to surgery, and two years post). 16% reported high levels of intrusive psychological distress and 8% reported high avoidance post pre and diagnosis. Predictors of distress: intrusive thoughts about dx, trait-anxiety, health complaints, problems sleeping (measured by health complaints check list). Sleep problems were correlated with intrusive psychological distress.
(Broeckel et al., 1998)	n=61				Compared to women with no cancer, adjuvant treated women reported more severe fatigue ($p<.01$), worse QOL ($p<.05$). Severe fatigue r/t poor sleep quality ($p<.05$), greater use of catastrophizing as a coping strategy, and presence of psychiatric disorder. Sleep problems a predictor of fatigue.
(Carpenter & Andrykowski, 1998)	n=155 bone marrow transplant n=56 renal transplant	Hot flashes Pain			Evaluated PSQI for cancer patients. Presented validity reliability data. Global sleep >=8 (higher then standard) indicates poor sleep and a predictor of fatigue.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
	n=102 BC n=159 benign changes				Mean score for BC=7.0 for global sleep.
Carpenter et al. 1999	N=114				Main variable: menopausal symptoms (prevalence and severity) in BCS. Interview of several symptoms check-lists-75% reported trouble sleeping.
(Carpenter & Elam, J. L. et al., 2004)	n=15 BCS n=15 healthy matched	Nighttime hot flashes			Primary variables: sleep, fatigue, hot flashes, depression. 73% BCS=poor sleep quality and high sleep disturbance with PSQI scores>=5. Sleep duration significantly shorter in BCS. No other significant group differences.
(Cimprich, 1999)	n=74 BC patients, newly diagnosed				Main variable: symptom distress in newly diagnosed BC patients. Reported insomnia via symptom distress scale: m=2.88 (30% of population reported symptoms of insomnia).

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Clark et al., 2004)	Sleep-wake w/cancer (review)	Pain	Cancer related distress		Sleep-wake disturbances are salient to cancer experience reported by patients. Includes nocturnal sleep and daytime sleepiness. Different prevalence rates by site specific cancers. Survival of cancer can be affected by the negative outcomes of sleep-wake disturbance. Noted relationships between age, gender, setting (hospitalization) for disturbances. Interventions include pharmacologic and non-pharmacologic. Regulated by the Two-Process Model of sleep regulation. Measured by subjective, objective measures. Phenomena requires multidisciplinary team approach for treatment.
(Couzi et al. 1995)	n=222 BC survey regarding attitudes of estrogen tx				Main variable: attitude toward estrogen replacement. Reported 44% complained of sleep disturbances.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Davidson et al., 2002)	N=982 cancer patients	Co-morbidities: (cardiovascular, respiratory, pain) Radiotherapy	Emotional/ physical distress at diagnosis		Sleep disturbances can lead to emotional, cognitive, physical dysfunction. Effective psychological interventions can improve negative consequences. 44% reported excessive fatigue. 41% reported restless leg. 31% reported symptoms of insomnia. 28% reported excessive sleepiness. 48%reorted insomnia prior or around time of cancer diagnosis.
(Deimling et al., 2002)	n=180 older adult, long-term cancer survivors, some BCS included				25% showed clinical levels of depression. Survivors displayed psychological distress r/t continued negative effects of cancer and treatment. Cancer-related symptoms predicted depression (b-0.27, $p<0.05$). Effects persist after even if stressors and non-cancer illness are controlled. Stressors: diagnosis, fear of recurrence, memories of trauma r/t dx or tx. Body image changes in BC=distress. Proposed conceptual model. Listed stressors but did not correlate with primary sleep variable. Insomnia was a negative consequence listed in the findings.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Dow et al., 1996)	n=294 BCS	Pain Sleep problems			Evaluated distress among BCS via subjective questionnaires. Fatigue, aches, pain, sleep problems persistent s/e after treatment. Over time: Psychological distress (fear of recurrence, metastatic disease), family distress, sexuality concerns, family burden, fear of uncertainty regarding future. Sleep an outcome, no predictors listed.
(Engstrom et al., 1999)	n=150 cancer patients (phase 1) n=42 cancer patients (phase 2)	Pain followed by emotional reaction that prevented further sleep Side effects of chemotherapy, medications	Psychological distress		44% report sleep problems during month prior to interview. ($x=5.82$; $p<.05$). 16% reported sleep problems to health care provider. Phase two: 45% reported sleep problems one month prior to interview (qualitative). 90% reported nighttime awakenings. People often attributed sleep problems as side effect of chemotherapy.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Fortner et al., 2002)	n=72 BC patients	Chemotherapy/radio-therapy side effects Chronic insomnia (occurring prior to cancer treatment) Lingering side effects of treatment Chronic pain	Depression due to diagnosis and treatment		61% had poor sleep quality. Sleep problems predict deficits in quality of life. Poor sleep causes deficits in work performance, daily task performance, physical limitations. Poor sleepers report lower energy levels for daily activities, daytime sleepiness, fatigue. Sleep has negative correlation with chemotherapy and radiotherapy. Breast cancer patients reporting poor sleep report increased emotional disturbances also contributing to decreased work performance, difficulty maintaining daily tasks, QOL. Disturbances: using bathroom, pain, awakenings, too hot. Suggests those with strong negative outlook on cancer diagnosis have worse sleep.
(Koopman et al., 2002)	n=97 BC metastatic disease	Cancer pain Education	Lack of social support Depressive symptoms		63% reported one or more sleep disturbance. 37% used sleeping pills. Sleep latency r/t pain and depressive symptoms. Nighttime awakenings r/t depression and low education. Morning awakenings problematic r/t depressive symptoms and less social support.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
					Daytime sleepiness did not have significant predictors. Decreased duration r/t metastases, bone pain, depressive symptoms, greater social support.
(Lee et al., 2004)	Sleep and cancer patients (review)	Individual differences in chronotype and circadian Gender, age, prior sleep history, Stage/type of cancer, Treatment side effects Other s/e: pain, apnea, narcolepsy, restless leg syndrome		Poor individual sleep hygiene Environment of sleep	Sleep is defined as multidimensional phenomena. Physiology of sleep cycle discussed (circadian pattern): 24 hr wake/sleep rhythm that allows normal human functioning. Sleep disturbance (insomnia): difficulty falling asleep, problems maintaining sleep, nighttime awakenings, excessive daytime sleepiness. Daytime sleepiness can mimic signs of fatigue. In breast cancer patients: tamoxifen side effects, menstrual/hormonal changes after treatment. Progressive disease states may lead to greater sleep disturbances. Medications prescribed for anxiety, depression, can cause increased reported sleep disturbances. Non-pharmacological interventions can be helpful but, initial accurate diagnosis of specific problem related to sleep (e.g., restless leg) is needed prior to intervention.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Miaskowski & Lee, 1999)	n=24 cancer patients with bone metastases	Low Karnofsky Performance scores (pain) High doses of radiotherapy			Main variable: sleep. 70% sleep efficiency per actigraphy (85% optimal for normal sleep). Pain is a predictor of fatigue and sleep disturbances. No correlations between objective measures and self-ratings of feeling rested and quality of sleep. 91% watch TV for self-care behavior 82% read.
(Mourits et al., 2002)	n=98 BC patients	Tamoxifen			Main variable: sexual well-being r/t tam use. 85% reported hot flashes. 55% reported sleep disturbance
(Northouse et al., 1999)	n=98 BCS	Sleep disturbances	Distress		Used stress/coping model for QOL in African American BC patients. Looked for predictors for increased QOL. Symptoms of distress were low. Problems reported were energy loss, sleep disturbance, pain. Explained QOL factors by means of appraisal (stress/coping model). Sleep disturbance was an antecedent to QOL.
(Okuyama et al., 2000)	n=134 BCS				Main variable: fatigue. Sleep was listed as significant correlate of fatigue. Dyspnea and depression also correlated with fatigue.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
					Three variables accounted for 46% variability.
(Redeker, Lev, & Ruggiero, 2000)	n=263 cancer patients	Radiation therapy			Sample undergoing chemotherapy. Main variables: insomnia, fatigue, depression, anxiety- positively correlated (r=.26 to r.69, p<.001). All negatively correlated with QOL (r=-.28 to r=-.63, p<.001). Women>men. Depression explained most of the 47% variance. Insomnia and fatigue explained only 4%. Age associated with increased QOL, less insomnia, fatigue, anxiety, depression. Sleep latency more intense in BC. 44-48% BC patients report sleep disturbance with radiotherapy.
(Roscoe et al., 2002)	n=78 BC patients	Circadian rhythm dysfunction			States sleep disturbances related to cancer can be alleviated by periods of rest. Circadian rhythms are endogenous, genetically based physiological 24 hr cyclic patterns. Cancer may alter circadian rhythms. Melatonin production (maintains sleep control), might be negatively correlated with BC.Central serotonin involved in sleep.No antecedents for sleep-wake disturbances listed.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
					States circadian rhythm disruption antecedent to depression and fatigue.
(Savard et al., 2001)	n=300 BC patients	Lumpectomy Chemotherapy Low tumor stage			Non-metastatic patients undergoing radiotherapy. 19% met criteria for insomnia syndrome. 95% of the insomnia cases were chronic. Onset: 33% prior to dx. 58% after diagnosis or aggravated by diagnosis. Risk: those on sick leave, unemployed, widowed, completed lumpectomy, chemotherapy, and had less severe cancer stage. Those with insomnia symptoms at risk for diagnosed syndrome: separated from spouse and had university degrees.
(Savard et al., 2004a)	n=24 BCS	Hot flashes			Variable: Hot flashes (objective) and sleep (PSG). Nights with hot flashes=lower Stage 2, longer REM latency, less efficient, more disrupted sleep.
(Servaes et al., 2002a)	n=57 fatigued BCS n=57 age-match chronic fatigue patients				Main variable: fatigue. BCS similar to CF in reporting psychological well-being, sleep and concentration.

		Predictors			
Author/Year	Sample	Physiological	Psychological	Environmental/ Sleep hygiene	Outcomes
(Spelten et al., 2003)	n=235 cancer patients post treatment				Main variable: how fatigue impacts time to return to work. Fatigue, diagnosis, treatment type, age, gender, depression, physical complaints (sleep) related to time to work return.
(Vena et al., 2004)	(review of all cancer patients)	lifestyle, disease-related, treatment-related	Psychological factors such as depression, anxiety		Main variable: Sleep is a passive state. Process regulated by behavioral, neuroendocrine, central nervous system factors. Sleep is a cyclic function with several stages and cycles (sleep architecture). Sleep disturbances diagnosed as: Dyssomnias. Parasomnias. Proposed sleep disorders.
(Weitzner et al., 2002)	n=13 BC patients with hot flashes	Hot flashes			Main variable: hot flashes. Tx with paroxetine. Improved sleep quality noted to be significant after intervention sing self report. Paired t-test showed M=0.77, SD 0.60 $p<0.0003$.

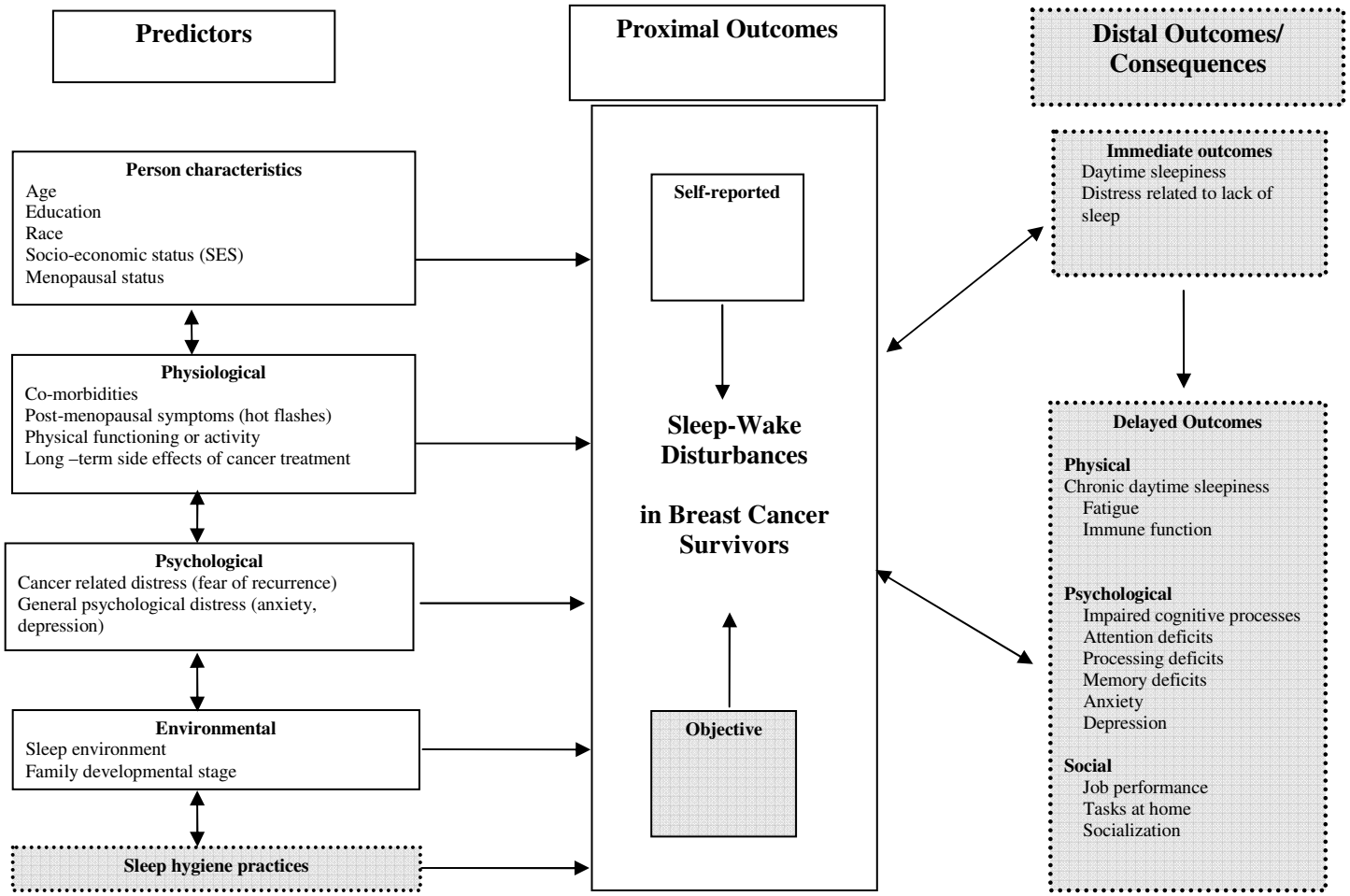
Theoretical models and measurement

Source	Theoretical framework	Measurement of sleep
Anderson, 2003	Did not specify	Sleep Disturbance Scale.
Andrykowski, 1998	Did not specify	PSQI.
Berger, 1998	Piper Integrated Fatigue Model (IFM)	Wrist actigraphy.
Berger, 1999	IFM	Wrist actigraphy.
Berger, 2000	IFM	Morin Sleep Diary. Wrist actigraphy.
Berger, 2003	IFM	Generic daily sleep diary. PSQI. Wrist actigraphy.
Bleiker, 2000	Did not specify	Symptom Check List-90 (SCL-90).
Broeckel, 1998	Did not specify	PSQI.
Carpenter, 1999	Did not specify	Symptom check-lists.
Carpenter, 1998	Did not specify	PSQI.
Carpenter, Elam et al., 2004	Lenz Model of Unpleasant Symptoms	PSQI.
Cimprich, 1999	Did not specify	Symptom distress scale.
Clark et al., 2004	Two Process Model	Review.
Couzi et al., 1995	Did not specify	Generic survey.
Davidson et al, 2002	Did not specify	Generic questionnaire.
Deimling, 2002	Stress and coping model for cancer survivors	None.
Dow, 1996	Quality of Life Model-adapted for cancer survivors	Symptom distress scale.
Engstrom, 1999	Did not specify	Telephone survey-generic sleep questions.
Fortner, 2002	Did not specify	PSQI.
Koopman, 2002	Did not specify	27-item Sleep Questionnaire (from a tool called Structured Insomnia Interview).
Miaskowski, 1999	Did not specify	Activity log. Generic sleep questions. Wrist actigraphy.
Mourits, 2002	Did not specify	Generic questions regarding sleep.
Northouse, 1999	Stress and coping framework	Inventory of Current Concerns.
Okuyama, 2000	Did not specify	Generic questions regarding sleep in demographics.

Source	Theoretical framework	Measurement of sleep
Redeker, 2000	Lenz Theory of Unpleasant Symptoms	Functional Assessment of Cancer Therapy.
Roscoe, 2002	Did not specify	Actigraph.
Savard, 2001	Spielman's Psychobiological Model	Insomnia Screening Questionnaire. Insomnia interview Schedule.
Savard, 2004	Did not specify	Insomnia Severity Index in Cancer Patients (ISI).
Servaes, 2002	Did not specify	Causal Attribution List (contains sleep subscale).
Spelten et al., 2003	Model of impact of cancer related symptoms	PSQI.
Vena et al., 2004	Two-process model of sleep	Review.
Weitzner et al., 2002	Did not specify	PSQI.

APPENDIX C

Elam Psychobiological Model Sleep-Wake Disturbances Model in Breast Cancer Survivors



APPENDIX D

Drugs that Effect Sleep

Drug Category	Drug	Sleep Disruption
Analgesics	Opioids	Decrease • REM • Stage II • arousal
	Nonsteroidal anti-inflammatory drugs	Increase • stage II Decrease • slow wave sleep Alters: thermoregulatory system
Antidepressants	Tricyclic	Decrease • REM • Total sleep time
	Selective serotonin reuptake	Decrease • REM • Total sleep time
Antiemetics	Dopamine antagonists	Increase • Drowsiness, sedation Decrease • REM
	Anticholinergic agents	Decrease • REM Increase • Stage II • Body movements
	5-HT3 antagonists	Increase • Drowsiness
Anxiolytics	Benzodiazepines	Decrease • slow wave sleep • REM Increase • Stage II Alters: thermoregulatory system
Corticosteroids	Prednisone and dexamethasone	Insomnia with bad dreams
Hypnotics	Benzodiazepines	Decrease • slow wave sleep • REM Increase • Stage II Alters: thermoregulatory system
	Non-benzodiazepines	Minimal effect on slow wave sleep and REM

Drug Category	Drug	Sleep Disruption
		Decrease • Sleep latency
Radiotherapy	None	Unknown
Chemotherapy	Anthracyclines	Unknown
	Taxanes	Unknown
Hormone Modulators	Tamoxifen	Unknown
	Aromotase Inhibitors	Unknown

*All drug effects have been noted with acute and chronic drug administration.

APPENDIX E

BCS and WWBC Measures

The following are snapshots from the measures used for the American Cancer Society Quality of Life Study (#RSGPB-04-089-01-PBP, Champion PI).

Medical Record Audit Form (MRAF)

1. Diagnosis and stage
    Date of diagnosis _____
    Initial stage _____
    T = _____ N = _____ M = _____
    T (1) < 2 cm _____T (2) 2.1 - 5.0 cm _____T (3) > 5 cm_____T (4) ___
    ER_____ PR_____ Her-2 Neu_____
    Local recurrence Y_____ No_____
    Systemic recurrence (except lymph nodes) Y_____N____
    Time since diagnosis (Date of diag - date of survey)_____
2. Treatment history- adjuvant therapy, reconstructive surgery, hormone therapy
    Surgery____
    Lumpectomy____
    Sential lymph node____
    Lymph node dissection____
    Simple mastectomy____
    Modified mastectomy____
    Completion mastectomy ____
    Type of reconstruction:
        None_____
        TRAM_____
        Latissimus Dorsi _____
        Implant _____
3. Systemic treatment
    Chemotherapy _____
    Drugs_____
    Adjuvant_____
    Neoadjuvant _____
    Tamoxifen _____ # yr _____
    AI _____# yr _____
    Herceptin _____
4. Radiation therapy _____

Questionnaire Number 9 9 9 9 9

Category 1 2

PERSONAL CHARACTERISTICS QUESTIONNAIRE
SURVIVOR

Please respond to the following questions by filling in the blanks or checking the best answer. All information will be kept confidential.

Individual Characteristics:

The following questions will help us describe women who are breast cancer survivors.

1. How would you describe your relationship at the time you were diagnosed with breast cancer?

[ ] Married or in a long-term committed relationship
[ ] Divorced
[ ] Widowed
[ ] Single

2. How would you describe your relationship now?

[ ] Married or in a long-term committed relationship (move on to question #3)
[ ] Divorced (skip to question #4)
[ ] Widowed (skip to question #7)
[ ] Single (skip to question #4)

3. Is this the same partner you had at the time of your diagnosis?

[ ] Yes (skip to questions #5 and #6)
[ ] No (move on to question #4)

4. Do you believe the decision to change your relationship was related to your breast cancer diagnosis or treatment?

[ ] Yes (skip to question #7)
[ ] No (skip to question #7)
[ ] I was not in a relationship at the time of my diagnosis/treatment. (skip to question #7)

If Yes, please explain:_____

_____

_____

PERSONAL CHARACTERISTICS QUESTIONNAIRE
SURVIVOR

The next two questions ask about any change in your relationship with your partner in general since your breast cancer diagnosis and treatment. If you were not with the same partner you had at diagnosis/treatment, please skip to question #7. Please CHECK the most appropriate answer.

5. Since being diagnosed with breast cancer, our relationship in general has:

[ ] Changed for the better
[ ] Stayed the same
[ ] Changed for the worse

6. Since having chemotherapy, our relationship in general has:

[ ] Changed for the better
[ ] Stayed the same
[ ] Changed for the worse

7a. Please **CIRCLE** the number of years of education you have completed, starting with 1st grade, which would be number 1):

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20+

7b. Please **CHECK** the highest level of education you have finished:

[ ] Graduate or professional degree
[ ] Some graduate school
[ ] Four-year College graduate (Bachelors Degree)
[ ] Two-year College graduate (Associates Degree)
[ ] Some college
[ ] Technical or Trade School
[ ] High school graduate/GED
[ ] Some high school
[ ] Elementary School or less

8. Do you consider yourself to be of Spanish/Hispanic/Latino origin:

[ ] NO [ ] YES

PERSONAL CHARACTERISTICS QUESTIONNAIRE
SURVIVOR

9. With which race do you identify yourself? Please **circle Yes or No for each option.**

Yes	No	White
Yes	No	Black or African American
Yes	No	Native Hawaiian or other Pacific Islander
Yes	No	Asian
Yes	No	American Indian or Alaskan native
Yes	No	Other race: _____

10. Is English your first language?

[ ] NO - If No, at what age did you begin to learn English? ☐☐
[ ] YES

11. What is your religious affiliation?

[ ] Christian, Catholic
[ ] Christian, not Catholic
[ ] Jewish
[ ] Islamic
[ ] Buddhist
[ ] No religious affiliation
[ ] Other; please specify:_____

12. Please choose the income category that matches your total household income for the last year, before taxes. This information is confidential.

[ ] < $15,000
[ ] $15,001 - $30,000
[ ] $30,001 - $50,000
[ ] $50,001 - $75,000
[ ] $75,001 - $100,000
[ ] $100,001 - $150,000
[ ] $150,001 - $200,000
[ ] > $200,000
[ ] Don't know

13. What is your current age? ☐☐

Questionnaire Number 9 9 9 9 9

Category 1 2

MEDICAL HISTORY QUESTIONNAIRE
SURVIVOR

Please respond to the following questions by filling in the blanks or checking the best answer. All information will be kept confidential and no individual information will be identified.

The following questions ask for information about your past health, medical and cancer history.

1. How old were you when you were diagnosed with breast cancer? ☐☐ years

2. How many months were you in initial treatment for breast cancer? This would mean surgery, chemotherapy and radiation. This does not include long-term medications (e.g. tamoxifen)

   ☐☐ months

3. Since completing treatment for breast cancer, have you had an illness or been involved in a serious accident requiring hospitalization?

   [ ] NO [ ] YES. Specify reason below (Check all that apply)

   [ ] Breast Cancer
   [ ] Other form of cancer, list:_____
   [ ] Other illness or surgery, list:_____
   [ ] Accident, list:_____
   [ ] Mental health, list:_____

4. What surgery did you have for breast cancer? [ ] Lumpectomy (skip to question #6)
   [ ] Mastectomy (move on to question #5)

5. Did you have reconstructive surgery? [ ] NO [ ] YES

6. Are you satisfied with this decision? [ ] NO [ ] YES

7. Have you ever been diagnosed or had a problem with any of the following? (Check all that apply.)

   [ ] Arthritis
   [ ] Heart disease or heart problem
   [ ] High blood pressure or hypertension
   [ ] Stroke
   [ ] Serious breathing disease or problem
   [ ] Kidney disease or problem
   [ ] High cholesterol
   [ ] Diabetes
   [ ] Leukemia or cancer (not breast cancer)
   [ ] Anxiety/panic disorders
   [ ] Depression
   [ ] Eating disorders
   [ ] Hip fracture
   [ ] Surgical replacement of joint
   [ ] Problem with urinary control
   [ ] Eye problems (other than corrective lenses)
   [ ] Hearing problems
   [ ] Other; Please specify:_____
   [ ] None

MEDICAL HISTORY QUESTIONNAIRE
SURVIVOR

8. How often do you currently drink alcoholic beverages?

[ ] Daily or almost every day
[ ] 3-4 times a week
[ ] Once or twice a week
[ ] Less than once a week
[ ] Never (skip to question #10)

9. On those days that you drink alcoholic beverages, about how many do you usually have?
(1 drink = 1 glass of wine/1 mixed drink/1 beer)

[ ] More than 5 drinks
[ ] 3 to 5 drinks
[ ] 1 to 2 drinks

10. Are you currently taking any medications for depression or anxiety? [ ] NO [ ] YES

11. What is your height? ☐ feet ☐☐ inches

12. What is your current weight? ☐☐☐ pounds

The next several questions are about your use of health care during the **past twelve months**.

13a. In the past twelve months, how many times have you seen your physician or other health care provider for:

1. *routine follow-up* for your breast cancer? ☐☐ number of times
2. a physical problem related to *having had breast cancer?* ☐☐ number of times
3. an annual checkup or a physical problem **not** related to *having had breast cancer?* ☐☐ number of times

13b. In the past twelve months, how many times have you gone to an emergency room for:

1. problems *related to having had breast cancer?* ☐☐ number of times
2. problems **not** related to having had breast cancer? ☐☐ number of times

13c. In the past twelve months, how many times have you seen a mental health professional/counselor?

☐☐ number of times

MEDICAL HISTORY QUESTIONNAIRE
SURVIVOR

14. How much were you involved in making decisions about your breast cancer?

[ ] Not at all [ ] Slightly [ ] Somewhat [ ] Completely

15. Who made most of the decisions regarding your breast cancer treatment?
(Please check only one answer)

[ ] Yourself
[ ] Parent(s)
[ ] Spouse or significant other
[ ] Close friend or relative
[ ] Your doctor
[ ] Other (Specify) _____

16. How satisfied are you with your involvement in decision-making about your breast cancer?

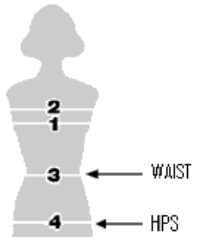
[ ] Not at all [ ] Slightly [ ] Somewhat [ ] Completely

17. Which of the following have you used since being diagnosed with breast cancer? For each service that you have used indicate if it was during treatment (D) or after treatment (A) by CIRCLING either A or D. Please also rate how helpful you felt this service was from (1) not helpful to (5) extremely helpful by CIRCLING one number.

Service	**When Used (D) During or (A) After**	**How Helpful (1) Not helpful to (5) Extremely Helpful**
Support group used for emotional support	D A	1 2 3 4 5
Support group used for information	D A	1 2 3 4 5
Internet used to get emotional support	D A	1 2 3 4 5
Internet used to get information	D A	1 2 3 4 5
Books/library	D A	1 2 3 4 5
Individual counseling	D A	1 2 3 4 5
Becoming involved with helping others	D A	1 2 3 4 5
Breast cancer activism	D A	1 2 3 4 5
Genetic counseling	D A	1 2 3 4 5
Genetic testing	D A	1 2 3 4 5
Seminars	D A	1 2 3 4 5

MEDICAL HISTORY QUESTIONNAIRE
SURVIVOR

We would now like for you to locate the measuring tape that was included in the package with your questionnaire and take a minute to measure your waist and hips. If possible, find a private spot to take these measurements so you can place the tape directly on your bare skin, not over your clothes.



18. First, wrap the tape around your waist at the smallest area between your belly button and your chest. Wrap the tape tight enough so there's no slack, but not too tight that it compresses your skin. If possible, check in a mirror to make sure the tape measure is straight (not angling up or down) around your waist. Relax, exhale, and record the measurement to the nearest inch.

Waist Measurement: ☐☐ inches

19. Now wrap the tape around the widest area of your buttocks. This is your hip measurement. As before, wrap the tape tight enough so there's no slack, but not too tight that it compresses your skin. If possible, check in a mirror to make sure the tape measure is straight (not angling up or down) around your buttocks. Relax, exhale, and record the measurement to the nearest inch.

Hip Measurement: ☐☐ inches

MEDICAL HISTORY QUESTIONNAIRE
SURVIVOR

20. For the last three months, which of the following activities have you performed regularly? (Please circle yes for all that apply and no if you do not perform the activity.)

		If Yes,
Play strenuous racquet sports (singles tennis, paddleball, etc.)	No Yes	☐☐ Hours/week
Play other strenuous sports (basketball, soccer, or other sports involving running.)	No Yes	☐☐ Hours/week
Ride a bicycle.	No Yes	☐☐ Hours/week
Swim.	No Yes	☐☐ Hours/week
Do you walk, run, or jog in your physical activity program?	No Yes	How many workouts per week? ☐☐ How many miles do you average per workout? ☐.☐ What is your average time per mile? ☐☐ minutes
How many times a week do you engage in vigorous physical activity long enough to work up a sweat?		☐☐ times/week

21. During the last seven days, how much time did you spend doing vigorous physical activity and moderate physical activity? Record only time actually engaged in the activity (ignore breaks, rest periods, etc.). Please do <u>not</u> record any *light* physical activity (office work, light housework, very light sports such as bowling, or any activities involving sitting). Record total hours below.

	Total hours for the last 7 days.
Vigorous activity (jogging or running, swimming, strenuous sports such as singles tennis or racquetball, digging in the garden, chopping wood, brisk walking, etc.)	☐☐ Total hours
Moderate activity (sports such as golf or doubles tennis, yard work, heavy house cleaning, bicycling on level ground, etc.)	☐☐ Total hours

MENSTRUAL AND GYNECOLOGICAL HISTORY
SURVIVOR

The following statements relate to your menstrual and gynecological history and to having children. Please **CIRCLE** the best answer or **FILL IN THE BLANKS**.

1. At what age did you begin having menstrual periods? ☐☐ years old

2. Please check the ONE statement that best describes you:

[ ] I have not had a menstrual period in the last 12 months. (Please also answer #2a.)
[ ] I have had a menstrual period in the last 12 months, but not in the last 3 months.
[ ] I have had a menstrual period in the last 3 months, but cycles are less regular.
[ ] I have had a menstrual period in the last 3 months, no change in regularity.

2a. Why did your periods stop?

[ ] Breast Cancer treatment
[ ] Normal aging
[ ] Medicine not related to breast cancer
[ ] Surgery (such as hysterectomy or ovaries removed)
[ ] Other, specify: _____
[ ] Don't know/Unsure

3. Have you had a hysterectomy (uterus or womb taken out)?

[ ] NO
[ ] YES. What year did you have the hysterectomy? ☐☐☐☐

4. Have you had your ovaries removed?

[ ] NO
[ ] YES, one ovary removed. If yes, what year was it removed? ☐☐☐☐
[ ] YES, both ovaries removed. If yes, what year were they removed? ☐☐☐☐

5. During the <u>past month</u>: Please indicate how true each statement has been for you by CIRCLING the number.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
a) I have had pelvic discomfort	1	2	3	4	5
b) I have had vaginal bleeding (between periods)	1	2	3	4	5
c) I have had a vaginal infection	1	2	3	4	5
d) I have had vaginal/vulvar irritation	1	2	3	4	5

MENSTRUAL AND GYNECOLOGICAL HISTORY
SURVIVOR

6. How many children did you have before being diagnosed with breast cancer? ☐☐

7. Do you have any children living with you now? [ ] NO [ ] YES

8. Do you feel that breast cancer prevented you from having all the children you wanted?

[ ] NO [ ] YES

9. Are you currently taking or using any of the following for menopausal symptoms? (check all that apply)

- [ ] Estrogen - oral
- [ ] Vitamin E
- [ ] Herbs
- [ ] Vaginal creams or lubricants
- [ ] Estrogen - vaginal (If checked, please specify below)
  - [ ] Vagifem
  - [ ] Estring
  - [ ] Estrogen Cream
- [ ] Antidepressants (Paxil, Effexor, etc)
- [ ] Other: _____
- [ ] None

10. Are you taking medications for sexual performance/desire? [ ] NO [ ] YES

11. Please mark one answer for each medication below. If you took a medication in the past or are still taking the medication, please tell us for how long.

	Never took this drug	Currently taking this drug	Took in the past but no longer taking	How many months did you take this drug?
Tamoxifen (Nolvadex)	1	2	3	☐☐ months
Raloxifen (Evista)	1	2	3	☐☐ months
Toremifene (Fareston)	1	2	3	☐☐ months
Fulvestran (Faslodex)	1	2	3	☐☐ months
Letrozole (Femara)	1	2	3	☐☐ months
Anastrozole (Arimidex)	1	2	3	☐☐ months
Exemestane (Aromasin)	1	2	3	☐☐ months
Trastuzumab (Herceptin)	1	2	3	☐☐ months
Birth Control Pills	1	2	3	☐☐☐ months

MENSTRUAL AND GYNECOLOGICAL HISTORY
SURVIVOR

12. During the past 4 weeks have you had hot flashes?

[ ] Yes
[ ] No (skip questions 13 and 14)

13. How often have you experienced hot flashes?

[ ] Once a week or less
[ ] Between 2 and 6 times per week
[ ] Daily
[ ] 2-3 times a day
[ ] 4 or more times a day

14. How much would you say your hot flashes bother you?

[ ] Not at all
[ ] Slightly
[ ] Moderately
[ ] Quite a bit
[ ] Extremely

PERFORMANCE 10 (PF10)
SURVIVOR

The following items are activities you might do during a typical day. Please **CIRCLE** one number on each line which indicates how your health now limits you in these activities.

	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
1. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
2. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf.	1	2	3
3. Lifting or carrying groceries.	1	2	3
4. Climbing **several** flights of stairs.	1	2	3
5. Climbing **one** flight of stairs.	1	2	3
6. Bending, kneeling, or stooping.	1	2	3
7. Walking **more than a mile**.	1	2	3
8. Walking **several blocks**.	1	2	3
9. Walking **one block**.	1	2	3
10. Bathing or dressing yourself.	1	2	3

PHYSICAL SYMPTOMS
SURVIVOR

Please tell us whether you think the following symptoms are of concern for breast cancer recurrence (your breast cancer returning) and should be reported to your healthcare team. Please **CIRCLE T** for true and **F** for false.

Symptom:		True	False
1.	Bone pain or tenderness lasting more than 2 weeks.	T	F
2.	Fever.	T	F
3.	Getting frequent colds.	T	F
4.	Skin rashes, redness, or swelling on your breast(s), breast scar, or chest area.	T	F
5.	New lumps or other changes in your breast(s), chest or scar areas.	T	F
6.	Flu-like symptoms (muscle aches, nausea, fever).	T	F
7.	Chest pain and any shortness of breath.	T	F
8.	Persistent hot flashes.	T	F
9.	Changes in sleep pattern.	T	F
10.	Persistent abdominal fullness/discomfort/pain.	T	F
11.	Changes in weight, especially weight loss.	T	F

PITTSBURGH SLEEP QUALITY INDEX (PSQI)
SURVIVOR

The following answers relate to your usual sleep habits **DURING THE PAST FOUR WEEKS**. Your answers should reflect the *majority* of days and nights during the **PAST FOUR WEEKS**.

1. During the PAST FOUR WEEKS, what time have you usually gone to bed at night?

☐☐:☐☐ AM/PM

2. During the PAST FOUR WEEKS, how long has it usually taken you to fall asleep at night?

☐☐☐ Number of minutes.

3. During the PAST FOUR WEEKS, what time have you usually gotten up in the morning?

☐☐:☐☐ AM/PM

4. During the PAST FOUR WEEKS, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

☐☐ Number of hours.

For each of the remaining questions, **CIRCLE** the one best response. Please answer all the questions.

DURING THE PAST FOUR WEEKS, how often have you had trouble sleeping because you...

	Not during the past 4 weeks	Less than once a week	Once or twice a week	Three or more times a week
5. Cannot get to sleep within 30 minutes.	1	2	3	4
6. Wake up in the middle of the night or early morning.	1	2	3	4
7. Have to get up to use the bathroom.	1	2	3	4
8. Cannot breathe comfortably.	1	2	3	4
9. Cough or snore loudly.	1	2	3	4
10. Feel too cold.	1	2	3	4
11. Feel too hot.	1	2	3	4
12. Have bad dreams.	1	2	3	4
13. Have pain.	1	2	3	4
14. Other reasons.	1	2	3	4

PITTSBURGH SLEEP QUALITY INDEX (PSQI)
SURVIVOR

15. During the PAST FOUR WEEKS how would you rate your sleep quality overall? (**CHECK ONE**)

[ ] Very Good
[ ] Fairly Good
[ ] Fairly Bad
[ ] Very Bad

16. During the PAST FOUR WEEKS, how often have you taken medicine (prescribed or "over the counter") to help you sleep? (**CHECK ONE**)

[ ] Not during the past 4 weeks
[ ] Less than once a week
[ ] Once or twice a week
[ ] Three or more times a week

17. During the PAST FOUR WEEKS, how often have you had trouble staying awake while driving, eating meals, or engaging in social activities? (**CHECK ONE**)

[ ] Not during the past 4 weeks
[ ] Less than once a week
[ ] Once or twice a week
[ ] Three or more times a week

18. During the PAST FOUR WEEKS, how much of a problem has it been for you to keep up enough enthusiasm to get things done? (**CHECK ONE**)

[ ] No problem at all
[ ] Only a very slight problem
[ ] Somewhat of a problem
[ ] A very big problem

19. Do you have a bed partner or roommate? (**CHECK ONE**)

[ ] No bed partner or roommate
[ ] Partner/roommate in other room
[ ] Partner/roommate in same room, but not in same bed
[ ] Partner in same bed

Questionnaire Number 9 9 9 9 9

Category 1 2

SYMPTOM CHECKLIST
SURVIVOR

We are interested in knowing about any sensations you may be feeling on the side of your body where you had your breast cancer treatment (surgery, radiation therapy).

CIRCLE yes or no for each symptom to indicate whether you have had the symptom DURING THE PAST WEEK. If you circle yes, please also circle one number to indicate how BOTHERED or DISTRESSED you were by the symptom.

0 = NOT AT ALL
1 = SLIGHTLY
2 = MODERATELY
3 = QUITE A BIT
4 = EXTREMELY

SYMPTOM / SENSATION	PRESENT		BOTHER / DISTRESS				
1. Arm feels heavy	NO	YES	0	1	2	3	4
2. Hand swollen	NO	YES	0	1	2	3	4
3. Arm swollen	NO	YES	0	1	2	3	4
4. Chest swollen	NO	YES	0	1	2	3	4
5. Arm feels tight	NO	YES	0	1	2	3	4
6. Arm feels hard	NO	YES	0	1	2	3	4
7. Burning sensations	NO	YES	0	1	2	3	4
8. Feel pins and needles (tingling)	NO	YES	0	1	2	3	4
9. Numbness	NO	YES	0	1	2	3	4
10. Breast pains	NO	YES	0	1	2	3	4
11. Skin crawls	NO	YES	0	1	2	3	4
12. Have you had to change your sleeping position because of any of these symptoms or sensations?	NO	YES	0	1	2	3	4

Questionnaire Number 9 9 9 9 9

Category 1 2

CES-D
SURVIVOR

Using the scale below, **CIRCLE** the number which best describes how often you felt or behaved this way **DURING THE PAST WEEK.**

No.	During the past week...	Rarely or none of the time (less than 1 day)	Some or little of the time (1-2 days)	Occasionally or a moderate amount of the time (3-4 days)	Most or all of the time (5-7 days)
1.	I was bothered by things that usually don't bother me.	1	2	3	4
2.	I did not feel like eating; my appetite was poor.	1	2	3	4
3.	I felt that I could not shake off the blues even with the help from my family or friends.	1	2	3	4
4.	I felt that I was just as good as other people.	1	2	3	4
5.	I had trouble keeping my mind on what I was doing.	1	2	3	4
6.	I felt depressed.	1	2	3	4
7.	I felt that everything I did was an effort.	1	2	3	4
8.	I felt hopeful about the future.	1	2	3	4
9.	I thought my life had been a failure.	1	2	3	4
10.	I felt fearful.	1	2	3	4
11.	My sleep was restless.	1	2	3	4
12.	I was happy.	1	2	3	4
13.	I talked less than usual.	1	2	3	4
14.	I felt lonely.	1	2	3	4
15.	People were unfriendly.	1	2	3	4
16.	I enjoyed life.	1	2	3	4
17.	I had crying spells.	1	2	3	4
18.	I felt sad.	1	2	3	4
19.	I felt that people disliked me.	1	2	3	4
20.	I could not get going.	1	2	3	4

Questionnaire Number 9 9 9 9 9

Category 1 2

CONCERNS ABOUT RECURRENCE
SURVIVOR

Although most women who have been diagnosed with early stage breast cancer will never have another problem with the cancer, we are aware that many women and their families do worry about this possibility. Your answers to these questions are very important to us.

The following questions ask about any worries you may have about the possibility of breast cancer recurrence. By recurrence we mean the breast cancer coming back in the same breast, another area of the body, or a new breast cancer in either breast.

For the following four questions please circle the number that comes closest to the way you feel. For example, for the first question you should circle "1" if you don't think about recurrence at all, circle "6" if you think about recurrence all the time, or circle "2", "3", "4" or "5" if the amount of time you spend thinking about recurrence is somewhere in between.

1. How much time do you spend **thinking** that your breast cancer could recur?

1	2	3	4	5	6
I Don't Think About It At All					*I Think About It All The Time*

2. How much does thinking that your breast cancer **could** recur **upset** you?

1	2	3	4	5	6
It Does not Upset Me At All					*It Makes Me Extremely Upset*

3. How often do you **worry** that your breast cancer could recur?

1	2	3	4	5	6
I Never Worry About It					*I Worry About It All The Time*

4. How **afraid** are you that your breast cancer may recur?

1	2	3	4	5	6
Not At All Afraid					*Very Afraid*

CONCERNS ABOUT RECURRENCE
SURVIVOR

*Now we are interested in what your concerns are regarding a possible recurrence of breast cancer. When thinking about the possibility of a recurrence **what is it** about that possibility that you worries you?*

*Although each of the following items may be a possibility of breast cancer recurrence, we are really interested in whether you **actually worry** about any of these things occurring. For example, you may believe that a recurrence of breast cancer could require further surgery. We would like to know whether you ever actually worry about this possibility.*

*For the following questions, please CIRCLE the number indicating **how much you worry** about each of the following items. If you do not worry about an item or if you think it does not apply to you, please circle "0" for "Not at All".*

I worry that a recurrence of my breast cancer would:	**Not at All**	**A little**	**Moderately**	**A lot**	**All or most of the time**
5. Upset me emotionally.	0	1	2	3	4
6. Keep me from doing the things I had planned to do.	0	1	2	3	4
7. Threaten my physical health.	0	1	2	3	4
8. Make me feel I am less of a woman.	0	1	2	3	4
9. Require chemotherapy.	0	1	2	3	4
10. Hurt my relationships with friends and family.	0	1	2	3	4
11. Make me feel that I don't have control over my life.	0	1	2	3	4
12. Threaten my identity (how I see myself).	0	1	2	3	4
13. Interfere with my physical ability to carry out daily activities.	0	1	2	3	4
14. Threaten my life.	0	1	2	3	4
15. Harm my self-confidence.	0	1	2	3	4
16. Be more serious than the first diagnosis.	0	1	2	3	4
17. Cause financial problems for me.	0	1	2	3	4
18. Interfere with my sense of sexuality.	0	1	2	3	4
19. Require radiation treatment.	0	1	2	3	4
20. Cause me pain and suffering.	0	1	2	3	4
21. Mean losing my breast(s).	0	1	2	3	4

CONCERNS ABOUT RECURRENCE SURVIVOR

I worry that a recurrence of my breast cancer would:	Not at All	A little	Moderately	A lot	All or most of the time
22. Interfere with my ability to plan for the future.	0	1	2	3	4
23. Threaten my spirituality or faith.	0	1	2	3	4
24. Keep me from fulfilling important roles (in my job or at home).	0	1	2	3	4
25. Lead me to feel less feminine.	0	1	2	3	4
26. Require further surgery.	0	1	2	3	4
27. Cause me to die.	0	1	2	3	4
28. Damage my romantic relationship(s).	0	1	2	3	4
29. Keep me from fulfilling my responsibilities (in my job or at home).	0	1	2	3	4
30. Make me feel badly about how my body looks or feels.	0	1	2	3	4
31. Harm my ability to be the parent I want to be.	0	1	2	3	4
32. Cause me to die and leave my children without a mother.	0	1	2	3	4

Please check any of the following events if they have happened one month before or you are expecting them to happen one month after you answer our questionnaire:

	Month Before	Month After
Appointment with healthcare providers.	[ ]	[ ]
Mammogram.	[ ]	[ ]
Helping other women with breast cancer through support groups or individual calls.	[ ]	[ ]
Anniversary of breast cancer diagnosis.	[ ]	[ ]
Breast Cancer fund raising events (Race for the Cure, Making Strides for Breast Cancer).	[ ]	[ ]
New symptoms I do not understand.	[ ]	[ ]
Blood work.	[ ]	[ ]

CONCERNS ABOUT RECURRENCE
SURVIVOR

Please CIRCLE the number that indicates the amount of time the following events have caused you to think about breast cancer **in the last month.**

	N/A	Not at All	A little	Moderately	A lot	All or most of the time
1. Breast Cancer fund raising events (Race for the Cure, Making Strides for Breast Cancer).	0	1	2	3	4	5
2. Helping other women with breast cancer through support groups or individual calls.	0	1	2	3	4	5
3. My annual date of diagnosis.	0	1	2	3	4	5
4. My mammogram.	0	1	2	3	4	5
5. New symptoms that I don't understand.	0	1	2	3	4	5
6. Hearing of someone I know who has had a recurrence of their breast cancer.	0	1	2	3	4	5
7. My routine oncologist (cancer doctor) appointment.	0	1	2	3	4	5
8. Blood work.	0	1	2	3	4	5
9. Other: _____	0	1	2	3	4	5
10. In general over the last month events that have made me think of breast cancer remind me how strong I am.	0	1	2	3	4	5
11. In general over the last month events that have made me think of breast cancer remind me of how frightened I am.	0	1	2	3	4	5

CONCERNS ABOUT RECURRENCE
SURVIVOR

12. I will have breast cancer recurrence during my life.

1	2	3	4	5
Strongly Disagree	**Disagree**	**Neither**	**Agree**	**Strongly Agree**

13. Do you know someone who has had a recurrence of their breast cancer?

[ ] YES (if yes, go to 14)
[ ] NO (Skip 14)

14. Knowing someone who had a recurrence of their breast cancer causes you to worry about a recurrence.

1	2	3	4	5
Strongly Disagree	**Disagree**	**Neither**	**Agree**	**Strongly Agree**

Questionnaire Number 9 9 9 9 9

Category 1 2

IMPACT OF EVENT SCALE-REVISED
SURVIVOR

Below is a list of difficulties people sometimes have after a stressful life situation. Please read each item, and then **CIRCLE** the number which indicates how distressing each has been for you **DURING THE PAST FOUR WEEKS** with respect to being diagnosed and treated for breast cancer.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Any reminder brought back feelings about breast cancer.	0	1	2	3	4
2. I had trouble staying asleep.	0	1	2	3	4
3. Other things kept making me think about breast cancer.	0	1	2	3	4
4. I felt irritable and angry.	0	1	2	3	4
5. I avoided letting myself get upset when I thought about breast cancer or was reminded of it.	0	1	2	3	4
6. I thought about breast cancer when I didn't mean to.	0	1	2	3	4
7. I felt as if having breast cancer hadn't happened or wasn't real.	0	1	2	3	4
8. I stayed away from reminders about breast cancer.	0	1	2	3	4
9. Pictures about breast cancer popped into my mind.	0	1	2	3	4
10. I was jumpy and easily startled.	0	1	2	3	4
11. I tried not to think about breast cancer.	0	1	2	3	4
12. I was aware that I still had a lot of feelings about having breast cancer, but I didn't deal with them.	0	1	2	3	4
13. I found myself acting or feeling as though I was back at the time of breast cancer diagnosis/treatment.	0	1	2	3	4
14. I had trouble falling asleep.	0	1	2	3	4
15. I had waves of strong feelings about having breast cancer.	0	1	2	3	4
16. I tried to remove breast cancer from my memory.	0	1	2	3	4
17. I had trouble concentrating.	0	1	2	3	4
18. I had dreams about breast cancer.	0	1	2	3	4
19. I felt watchful or on guard.	0	1	2	3	4
20. I tried not to think about breast cancer.	0	1	2	3	4

Questionnaire Number 9 9 9 9 9

Category 1 2

SELF-EVALUATION QUESTIONNAIRE
SURVIVOR

STAI Form Y-1

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel **right now**, that is, ***at this moment***. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	Not at All	Somewhat	Moderately So	Very Much So
1. I feel calm.	1	2	3	4
2. I feel secure.	1	2	3	4
3. I am tense.	1	2	3	4
4. I feel strained.	1	2	3	4
5. I feel at ease.	1	2	3	4
6. I feel upset.	1	2	3	4
7. I am presently worrying over possible misfortunes.	1	2	3	4
8. I feel satisfied.	1	2	3	4
9. I feel frightened.	1	2	3	4
10. I feel comfortable.	1	2	3	4
11. I feel self-confident.	1	2	3	4
12. I feel nervous.	1	2	3	4
13. I am jittery.	1	2	3	4
14. I feel indecisive.	1	2	3	4
15. I am relaxed.	1	2	3	4
16. I feel content.	1	2	3	4
17. I am worried.	1	2	3	4
18. I feel confused.	1	2	3	4
19. I feel steady.	1	2	3	4
20. I feel pleasant.	1	2	3	4

Questionnaire Number

Category

SELF-EVALUATION QUESTIONNAIRE
SURVIVOR

STAI Form Y-2

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you ***generally*** feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	Almost Never	Sometimes	Often	Almost Always
21. I feel pleasant.	1	2	3	4
22. I feel nervous and restless.	1	2	3	4
23. I feel satisfied with myself.	1	2	3	4
24. I wish I could be as happy as others seem to be.	1	2	3	4
25. I feel like a failure.	1	2	3	4
26. I feel rested.	1	2	3	4
27. I am "calm, cool, and collected".	1	2	3	4
28. I feel that difficulties are piling up so that I cannot overcome them.	1	2	3	4
29. I worry too much over something that really doesn't matter.	1	2	3	4
30. I am happy.	1	2	3	4
31. I have disturbing thoughts.	1	2	3	4
32. I lack self-confidence.	1	2	3	4
33. I feel secure.	1	2	3	4
34. I make decisions easily.	1	2	3	4
35. I feel inadequate.	1	2	3	4
36. I am content.	1	2	3	4
37. Some unimportant thought runs through my mind and bothers me.	1	2	3	4
38. I take disappointments so keenly that I can't put them out of my mind.	1	2	3	4
39. I am a steady person.	1	2	3	4
40. I get in a state of tension or turmoil as I think over my recent concerns and interests.	1	2	3	4

APPENDIX F

Age-Matched WWBC Measures

Questionnaire Number 9 9 9 9 9

Category 5

PERSONAL CHARACTERISTICS QUESTIONNAIRE
ACQUAINTANCE CONTROL

Please respond to the following questions by filling in the blanks or checking the best answer.
All information will be kept confidential.

Individual Characteristics:

The following questions will help us describe women who do not have a history of breast cancer.

1. How would you describe your relationship five years ago?

[ ] Married or in a long-term committed relationship
[ ] Divorced
[ ] Widowed
[ ] Single

2. How would you describe your relationship now?

[ ] Married or in a long-term committed relationship (move on to question #3)
[ ] Divorced (skip to question #4)
[ ] Widowed (skip to question #4)
[ ] Single (skip to question #4)

3. Is this the same partner you had five years ago?

[ ] Yes
[ ] No

4a. Please **CIRCLE** the number of years of education you have completed, starting with 1st grade, which would be number 1:

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20+

4b. Please **CHECK** the highest level of education you have finished:

[ ] Graduate or professional degree
[ ] Some graduate school
[ ] Four-year College graduate (Bachelors Degree)
[ ] Two-year College graduate (Associates Degree)
[ ] Some college
[ ] Technical or Trade School
[ ] High school graduate/GED
[ ] Some high school
[ ] Elementary School or less

PERSONAL CHARACTERISTICS QUESTIONNAIRE
ACQUAINTANCE CONTROL

5. Do you consider yourself to be of Spanish/Hispanic/Latino origin:

[ ] NO [ ] YES

6. With which race do you identify yourself? Please **circle Yes or No for each option.**

Yes	No	White
Yes	No	Black or African American
Yes	No	Native Hawaiian or other Pacific Islander
Yes	No	Asian
Yes	No	American Indian or Alaskan native
Yes	No	Other race: _____

7. Is English your first language?

[ ] NO - If No, at what age did you begin to learn English? ☐☐

[ ] YES

8. What is your religious affiliation?

[ ] Christian, Catholic
[ ] Christian, not Catholic
[ ] Jewish
[ ] Islamic
[ ] Buddhist
[ ] No religious affiliation
[ ] Other; please specify:_____

9. Please choose the income category that matches your total household income for the last year, before taxes. This information is confidential.

[ ] < $15,000
[ ] $15,001 - $30,000
[ ] $30,001 - $50,000
[ ] $50,001 - $75,000
[ ] $75,001 - $100,000
[ ] $100,001 - $150,000
[ ] $150,001 - $200,000
[ ] > $200,000
[ ] Don't know

10. What is your current age? ☐☐

Questionnaire Number 9 9 9 9 9

Category 5

MEDICAL HISTORY QUESTIONNAIRE
ACQUAINTANCE CONTROL

Please respond to the following questions by filling in the blanks or checking the best answer. All information will be kept confidential and no individual information will be identified.

The following questions ask for information about your past health and medical history.

1. Have you ever been diagnosed or had a problem with any of the following? (Check all that apply.)

[ ] Arthritis
[ ] Heart disease or heart problem
[ ] High blood pressure or hypertension
[ ] Stroke
[ ] Serious breathing disease or problem
[ ] Kidney disease or problem
[ ] High cholesterol
[ ] Diabetes
[ ] Leukemia or cancer (not breast cancer)
[ ] Anxiety/panic disorders
[ ] Depression
[ ] Eating disorders
[ ] Hip fracture
[ ] Surgical replacement of joint
[ ] Problem with urinary control
[ ] Eye problems (other than corrective lenses)
[ ] Hearing problems
[ ] Other; Please specify: _____
[ ] None

2. How often do you currently drink alcoholic beverages?

[ ] Daily or almost every day
[ ] 3-4 times a week
[ ] Once or twice a week
[ ] Less than once a week
[ ] Never (skip to question #4)

3. On those days that you drink alcoholic beverages, about how many do you usually have? (1 drink = 1 glass of wine/1 mixed drink/1 beer)

[ ] More than 5 drinks
[ ] 3 to 5 drinks
[ ] 1 to 2 drinks

4. What is your height? ☐ feet ☐☐ inches

5. What is your current weight? ☐☐☐ pounds

MEDICAL HISTORY QUESTIONNAIRE
ACQUAINTANCE CONTROL

6. In the past 12 months:

a. How many times have you seen your physician or other health care provider for a physical problem? [ ][ ] number of times

b. How many times have you gone to the emergency room? [ ][ ] number of times

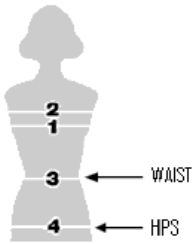
c. How many days have you spent in the hospital? [ ][ ] number of days

d. How many times have you seen a mental health professional/counselor? [ ][ ] number of times

7. Who makes most of the decisions regarding your health care? (Please check only one answer)

[ ] Yourself
[ ] Parent(s)
[ ] Spouse or significant other
[ ] Close friend or relative
[ ] Your doctor
[ ] Other (Specify)_____

We would now like for you to locate the measuring tape that was included in the package with your questionnaire and take a minute to measure your waist and hips. If possible, find a private spot to take these measurements so you can place the tape directly on your bare skin, not over your clothes.



8. First, wrap the tape around your waist at the smallest area between your belly button and your chest. Wrap the tape tight enough so there's no slack, but not too tight that it compresses your skin. If possible, check in a mirror to make sure the tape measure is straight (not angling up or down) around your waist. Relax, exhale, and record the measurement to the nearest inch.

Waist Measurement: [ ][ ] inches

MEDICAL HISTORY QUESTIONNAIRE
ACQUAINTANCE CONTROL

9. Now wrap the tape around the widest area of your buttocks. This is your hip measurement. As before, wrap the tape tight enough so there's no slack, but not too tight that it compresses your skin. If possible, check in a mirror to make sure the tape measure is straight (not angling up or down) around your buttocks. Relax, exhale, and record the measurement to the nearest inch.

Hip Measurement: ☐☐ inches

10. For the last three months, which of the following activities have you performed regularly? (Please circle yes for all that apply and no if you do not perform the activity.)

		If Yes,
Play strenuous racquet sports (singles tennis, paddleball, etc.)	No Yes	☐☐ Hours/week
Play other strenuous sports (basketball, soccer, or other sports involving running.)	No Yes	☐☐ Hours/week
Ride a bicycle.	No Yes	☐☐ Hours/week
Swim.	No Yes	☐☐ Hours/week
Do you walk, run, or jog in your physical activity program?	No Yes	How many workouts per week? ☐☐ How many miles do you average per workout? ☐.☐ What is your average time per mile? ☐☐ minutes
How many times a week do you engage in vigorous physical activity long enough to work up a sweat?		☐☐ times/week

11. During the last seven days, how much time did you spend doing vigorous physical activity and moderate physical activity? Record only time actually engaged in the activity (ignore breaks, rest periods, etc.). Please do not record any *light* physical activity (office work, light housework, very light sports such as bowling, or any activities involving sitting). Record total hours below.

	Total hours for the last 7 days.
Vigorous activity (jogging or running, swimming, strenuous sports such as singles tennis or racquetball, digging in the garden, chopping wood, brisk walking, etc.)	☐☐ Total hours
Moderate activity (sports such as golf or doubles tennis, yard work, heavy house cleaning, bicycling on level ground, etc.)	☐☐ Total hours

MENSTRUAL AND GYNECOLOGICAL HISTORY
ACQUAINTANCE CONTROL

The following statements relate to your menstrual and gynecological history and to having children. Please **CIRCLE** the best answer or **FILL IN THE BLANKS**.

1. At what age did you begin having menstrual periods? ☐☐ years old

2. Please check the ONE statement that best describes you:

[ ] I have not had a menstrual period in the last 12 months. (Please also answer #2a.)

[ ] I have had a menstrual period in the last 12 months, but not in the last 3 months.

[ ] I have had a menstrual period in the last 3 months, but cycles are less regular.

[ ] I have had a menstrual period in the last 3 months, no change in regularity.

2a. Why did your periods stop?

[ ] Normal aging
[ ] Medication
[ ] Surgery (such as hysterectomy or ovaries removed)
[ ] Other, specify:
[ ] Don't know/Unsure _____

3. Have you had a hysterectomy (uterus or womb taken out)?

[ ] NO

[ ] YES. What year did you have the hysterectomy? ☐☐☐☐

4. Have you had your ovaries removed?

[ ] NO

[ ] YES, one ovary removed. If yes, what year was it removed? ☐☐☐☐

[ ] YES, both ovaries removed. If yes, what year were they removed? ☐☐☐☐

5. During the <u>past month</u>: Please indicate how true each statement has been for you by CIRCLING the number.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
a) I have had pelvic discomfort	1	2	3	4	5
b) I have had vaginal bleeding (between periods)	1	2	3	4	5
c) I have had a vaginal infection	1	2	3	4	5
d) I have had vaginal/vulvar irritation	1	2	3	4	5

MENSTRUAL AND GYNECOLOGICAL HISTORY
ACQUAINTANCE CONTROL

6. Do you feel that you are or have been physically able to have all the children you wanted?

[ ] NO [ ] YES

7. How many children have you had? ☐☐ children

8. Do you have any children living with you now? [ ] NO [ ] YES

9. Are you currently pregnant?

[ ] NO
[ ] YES, I'm currently ☐☐ weeks pregnant

10. Are you currently taking or using any of the following for menopausal symptoms? (check all that apply)

[ ] Estrogen - oral
[ ] Vitamin E
[ ] Herbs
[ ] Vaginal creams or lubricants
[ ] Estrogen - vaginal (If checked, please specify below)
  [ ] Vagifem
  [ ] Estring
  [ ] Estrogen Cream
[ ] Antidepressants (Paxil, Effexor, etc)
[ ] Other: _____
[ ] None

11. Are you taking medications for sexual performance/desire?

[ ] NO [ ] YES

12. Please mark one answer for each medication below. If you took a medication in the past or are still taking the medication, please tell us for how long.

	Never took this drug	Currently taking this drug	Took in the past but no longer taking	How many months did you take this drug?
Tamoxifen (Nolvadex)	1	2	3	☐☐ months
Raloxifen (Evista)	1	2	3	☐☐ months
Birth Control Pills	1	2	3	☐☐☐ months

MENSTRUAL AND GYNECOLOGICAL HISTORY
ACQUAINTANCE CONTROL

13. During the past 4 weeks have you had hot flashes?

[ ] Yes
[ ] No (skip questions 14 and 15)

14. How often have you experienced hot flashes?

[ ] Once a week or less
[ ] Between 2 and 6 times per week
[ ] Daily
[ ] 2-3 times a day
[ ] 4 or more times a day

15. How much would you say your hot flashes bother you?

[ ] Not at all
[ ] Slightly
[ ] Moderately
[ ] Quite a bit
[ ] Extremely

PERFORMANCE 10 (PF10)
ACQUAINTANCE CONTROL

The following items are activities you might do during a typical day. Please **CIRCLE** one number on each line which indicates how your health now limits you in these activities.

	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
1. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
2. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf.	1	2	3
3. Lifting or carrying groceries.	1	2	3
4. Climbing **several** flights of stairs.	1	2	3
5. Climbing **one** flight of stairs.	1	2	3
6. Bending, kneeling, or stooping.	1	2	3
7. Walking **more than a mile**.	1	2	3
8. Walking **several blocks**.	1	2	3
9. Walking **one block**.	1	2	3
10. Bathing or dressing yourself.	1	2	3

Questionnaire Number 9 9 9 9 9

Category 5

PITTSBURGH SLEEP QUALITY INDEX (PSQI)
ACQUAINTANCE CONTROL

The following answers relate to your usual sleep habits **DURING THE PAST FOUR WEEKS**. Your answers should reflect the *majority* of days and nights during the **PAST FOUR WEEKS**.

1. During the PAST FOUR WEEKS, what time have you usually gone to bed at night?

☐☐ : ☐☐ AM/PM

2. During the PAST FOUR WEEKS, how long has it usually taken you to fall asleep at night?

☐☐☐ Number of minutes.

3. During the PAST FOUR WEEKS, what time have you usually gotten up in the morning?

☐☐ : ☐☐ AM/PM

4. During the PAST FOUR WEEKS, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

☐☐ Number of hours.

For each of the remaining questions, **CIRCLE** the one best response. Please answer all the questions.

DURING THE PAST FOUR WEEKS, how often have you had trouble sleeping because you...

	Not during the past 4 weeks	Less than once a week	Once or twice a week	Three or more times a week
5. Cannot get to sleep within 30 minutes.	1	2	3	4
6. Wake up in the middle of the night or early morning.	1	2	3	4
7. Have to get up to use the bathroom.	1	2	3	4
8. Cannot breathe comfortably.	1	2	3	4
9. Cough or snore loudly.	1	2	3	4
10. Feel too cold.	1	2	3	4
11. Feel too hot.	1	2	3	4
12. Have bad dreams.	1	2	3	4
13. Have pain.	1	2	3	4
14. Other reasons.	1	2	3	4

PITTSBURGH SLEEP QUALITY INDEX (PSQI)
ACQUAINTANCE CONTROL

15. During the PAST FOUR WEEKS how would you rate your sleep quality overall? (**CHECK ONE**)

[ ] Very Good
[ ] Fairly Good
[ ] Fairly Bad
[ ] Very Bad

16. During the PAST FOUR WEEKS, how often have you taken medicine (prescribed or "over the counter") to help you sleep? (**CHECK ONE**)

[ ] Not during the past 4 weeks
[ ] Less than once a week
[ ] Once or twice a week
[ ] Three or more times a week

17. During the PAST FOUR WEEKS, how often have you had trouble staying awake while driving, eating meals, or engaging in social activities? (**CHECK ONE**)

[ ] Not during the past 4 weeks
[ ] Less than once a week
[ ] Once or twice a week
[ ] Three or more times a week

18. During the PAST FOUR WEEKS, how much of a problem has it been for you to keep up enough enthusiasm to get things done? (**CHECK ONE**)

[ ] No problem at all
[ ] Only a very slight problem
[ ] Somewhat of a problem
[ ] A very big problem

19. Do you have a bed partner or roommate? (**CHECK ONE**)

[ ] No bed partner or roommate
[ ] Partner/roommate in other room
[ ] Partner/roommate in same room, but not in same bed
[ ] Partner in same bed

CES-D
ACQUAINTANCE CONTROL

Using the scale below, **CIRCLE** the number which best describes how often you felt or behaved this way **DURING THE PAST WEEK.**

No.	During the past week...	Rarely or none of the time (less than 1 day)	Some or little of the time (1-2 days)	Occasionally or a moderate amount of the time (3-4 days)	Most or all of the time (5-7 days)
1.	I was bothered by things that usually don't bother me.	1	2	3	4
2.	I did not feel like eating; my appetite was poor.	1	2	3	4
3.	I felt that I could not shake off the blues even with the help from my family or friends.	1	2	3	4
4.	I felt that I was just as good as other people.	1	2	3	4
5.	I had trouble keeping my mind on what I was doing.	1	2	3	4
6.	I felt depressed.	1	2	3	4
7.	I felt that everything I did was an effort.	1	2	3	4
8.	I felt hopeful about the future.	1	2	3	4
9.	I thought my life had been a failure.	1	2	3	4
10.	I felt fearful.	1	2	3	4
11.	My sleep was restless.	1	2	3	4
12.	I was happy.	1	2	3	4
13.	I talked less than usual.	1	2	3	4
14.	I felt lonely.	1	2	3	4
15.	People were unfriendly.	1	2	3	4
16.	I enjoyed life.	1	2	3	4
17.	I had crying spells.	1	2	3	4
18.	I felt sad.	1	2	3	4
19.	I felt that people disliked me.	1	2	3	4
20.	I could not get going.	1	2	3	4

Section 6:
Questions Specific to a Stressful event in the last 5 years

The next several questionnaires focus on your experiences with a stressful event in the last 5 years. The measures in this section assess coping, emotional adjustment, social support, and other important factors. When completing each of the following questionnaires please consider a stressful event in your life and carefully read the directions at the top of each page.

Examples of stressful events might be:

- A serious personal illness (diabetes)
- Illness of a family member such as a child or parent
- Loss of a loved one
- Loss of a job
- Major relationship change (divorce, break up of a long-term relationship)

IMPACT OF EVENT SCALE-REVISED
ACQUAINTANCE CONTROL

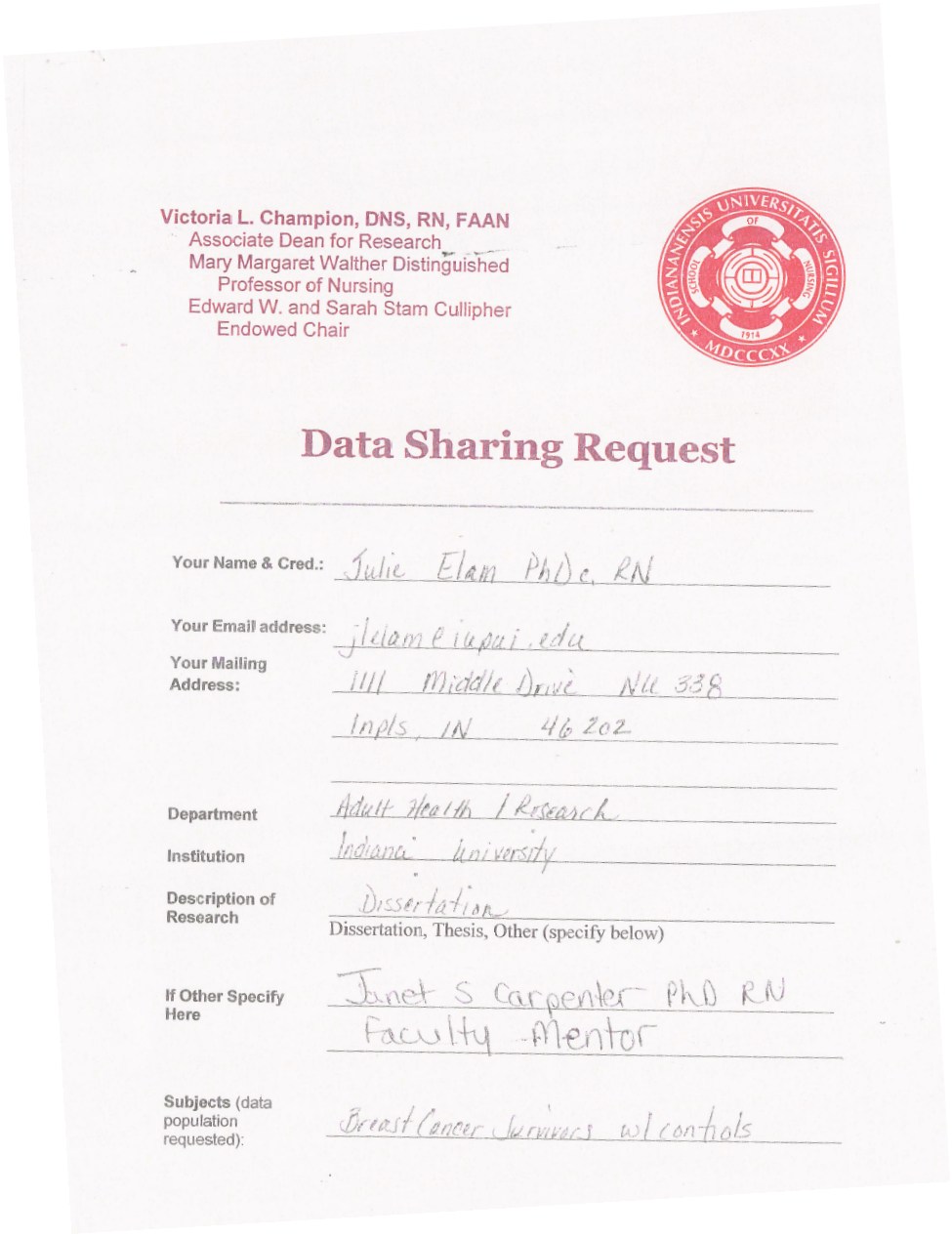
Below is a list of difficulties people sometimes have after a stressful life situation. Please read each item, and then **CIRCLE** the number which indicates how distressing each has been for you **DURING THE PAST FOUR WEEKS** with respect to a stressful life event.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Any reminder brought back feelings about the stressful event.	0	1	2	3	4
2. I had trouble staying asleep.	0	1	2	3	4
3. Other things kept making me think about the stressful event.	0	1	2	3	4
4. I felt irritable and angry.	0	1	2	3	4
5. I avoided letting myself get upset when I thought about the stressful event or was reminded of it.	0	1	2	3	4
6. I thought about the stressful event when I didn't mean to.	0	1	2	3	4
7. I felt as if the stressful event hadn't happened or wasn't real.	0	1	2	3	4
8. I stayed away from reminders about the stressful event.	0	1	2	3	4
9. Pictures about the stressful event popped into my mind.	0	1	2	3	4
10. I was jumpy and easily startled.	0	1	2	3	4
11. I tried not to think about the stressful event.	0	1	2	3	4
12. I was aware that I still had a lot of feelings about the stressful event, but I didn't deal with them.	0	1	2	3	4
13. I found myself acting or feeling as though I was back at the time of the stressful event.	0	1	2	3	4
14. I had trouble falling asleep.	0	1	2	3	4
15. I had waves of strong feelings about the stressful event.	0	1	2	3	4
16. I tried to remove the stressful event from my memory.	0	1	2	3	4
17. I had trouble concentrating.	0	1	2	3	4
18. I had dreams about the stressful event.	0	1	2	3	4
19. I felt watchful or on guard.	0	1	2	3	4
20. I tried not to think about the stressful event.	0	1	2	3	4

APPENDIX E

Regulatory Information

Data sharing agreements



Victoria L. Champion, DNS, RN, FAAN
Associate Dean for Research
Mary Margaret Walther Distinguished Professor of Nursing
Edward W. and Sarah Stam Cullipher Endowed Chair

INDIANANENSIS UNIVERSITATIS SIGILLUM
SCHOOL OF NURSING
1914
MDCCCXX

Data Sharing Request

Your Name & Cred.: Julie Elam PhDc, RN

Your Email address: jlelam@iupui.edu

Your Mailing Address: 1111 Middle Drive NU 338
Inpls, IN 46202

Department: Adult Health / Research

Institution: Indiana University

Description of Research: Dissertation
Dissertation, Thesis, Other (specify below)

If Other Specify Here: Janet S Carpenter PhD RN
Faculty Mentor

Subjects (data population requested): Breast Cancer Survivors w/ controls

Location
(where research will be carried out): Indiana University

Name of parent study for which data is requested: Quality of Life in Younger Breast Cancer Survivors (PI- Dr. Victoria Champion)

Funding Source: American Cancer Society (# RSG PB-04-089-01-PBP)

Permission is requested to obtain data (specify variable) for the research project described above: Predictors of Sleep-Wake Disturbances in BCS (See attached) and controls

Research Question: (Question and analysis plan is to be included) See attached

Other Request's (please specify here.)

By submitting this document you must agree to the following:

1. I agree to send a copy of the thesis or dissertation proposal to Center for Research and Scholarship, 1111 Middle Drive, NU 340 G, Indianapolis, IN 46202-5107
2. All data or scales will be used in accordance with the Code of Ethics of the American Psychological Association.
3. I agree to provide a detailed description of my procedures and results as soon as possible after the completion of the research.
4. I agree that whenever data is presented in any fashion that the grant title, funding agency, and principal investigator is acknowledged and included in authorship as specified un[illegible]

Feb 1, 2007
Approval Date:

Signature

Location
(where research will be carried out): Indiana University

Name of parent study for which data is requested: Survey of Quality of Life in Women
(PI) Kathy Russell PhD

Funding Source: NIH (#R03CA-097737) & Walther Cancer Institute

Permission is requested to obtain data (specify variable) for the research project described above: Predictor variables of Sleep-wake disturbances in Breast Cancer Survivors and controls

Research Question:
(Question and analysis plan is to be included) see attached

Other Request's
(please specify here.)

By submitting this document you must agree to the following:

1. I agree to send a copy of the thesis or dissertation proposal to Center for Research and Scholarship, 1111 Middle Drive, NU 340 G, Indianapolis, IN 46202-5107
2. All data or scales will be used in accordance with the Code of Ethics of the American Psychological Association.
3. I agree to provide a detailed description of my procedures and results as soon as possible after the completion of the research.
4. I agree that whenever data is presented in any fashion that the grant title, funding agency, and principal investigator is acknowledged and included in authorship as specified under Guideline for Using Grant Data

2-6-07
Approval Date:

Signature

IRB approval

IUPUI AND CLARIAN INSTITUTIONAL REVIEW BOARD

CONTINUING REVIEW (IRB-01)

DUE DATE: Dec. 14, 2007 IRB STUDY NUMBER: **0702-69B**

Principal Investigator: Janet Carpenter, PhD, RN **Department: Adult Health**

Building Room No.: NU340D Phone: 317-278-6093 E-Mail: carpentj@iupui.edu

Contact Information: Name: Julie Elam Address: NU 338

Phone: 317-278-6095 Fax: 317-278-2021 E-Mail: jlelam@iupui.edu

Study Title: **Predictors of Sleep-Wake Disturbances in Breast Cancer Survivors Compared to Women without Breast Cancer**

Sponsor/Funding Agency: National Institutes of Nursing Research Grant/Sponsor No.: 5F31NR009890-02/

SECTION I: CURRENT STUDY STATUS

The study status must be ONGOING if either of the 2 is true: (1) Interaction or intervention with subjects, including follow-up, continues and/or (2) Identifiable private information is being accessed.

- ☐ ONGOING – Date initiated
- ☐ ONGOING – Will be initiated, Anticipated date:
  (Skip to Section IV and complete the rest of the form)
- ☒ ONGOING – Permanently closed to subject enrollment, DATA ANALYSIS ONLY (NOTE: If you and/or the sponsor will require access to private, identifiable information, the study must remain "ONGOING." If however, the sponsor is doing data analysis only and will not require you to access private, identifiable information or contact with subjects, you may request that the study be considered "COMPLETED" – see below).
- ☐ ONGOING – Permanently closed to subject enrollment, RESEARCH INTERACTION OR INTERVENTION CONTINUES (this includes follow-up)
  - ☐ Check here if subjects will be required to reconsent and/or reauthorize. (You will need to attach the current informed consent and authorization with this continuing review form).
  - ☐ Check here if subjects will NOT be required to reconsent and/or reauthorize and to certify that the information provided in the summary safeguard statement (SSS), which must be attached with this continuing review form, is up-to-date and accurate.
- ☐ WILL NOT BE INITIATED – Explain: _____
  (Skip to investigator signature under Section VI)
- ☐ COMPLETED – Date:
- ☐ CLOSED PRIOR TO COMPLETION – Date: __, Explain: _____

If applicable, explain what will happen to samples/tissues/data collected as part of the research study: _____

SECTION II: SUBJECT SUMMARY

☐ Check here if your study utilizes records or specimens versus human subjects. When the form asks for the number of subjects, document the number of subjects for which data/specimens have been collected.

1. ACCRUAL-n/a Retrospective data analysis for dissertation-no subjects were recruited.

			All Sites	On-Site
Projected		Number of subjects approved by the IRB (see section III.C of SSS)	n/a	n/a
Actual	Since last IRB review	Number of subjects **CONSENTED/ENROLLED**		n/a
		Number of subjects who **FAILED SCREENING** (e.g. found ineligible to participate)		n/a
		Number of subjects who have **WITHDRAWN** from the study		n/a

Checklist of Required Revisions at the Time of Continuing Review

(Rev 01/07)

IRB Study #: **0702-69B**

Please read the instructions below to ensure that you submit complete paperwork with your continuing review. Otherwise, you may experience delays in your study receiving approval.

☐ **ONGOING – Date initiated**
☐ **ONGOING – Will be initiated**

If you select either of these study statuses under Section I of the continuing review form, you must update the study's summary safeguard statement to the 06/05 or 08/05 version. The most current version can be found at: http://www.iupui.edu/%7Eresgrad/spon/download2.htm.

☒ **ONGOING – Date initiated 6/15/2007**
☐ **ONGOING – Will be initiated**
☐ **ONGOING – Permanently closed to subject enrollment, and subjects will be required to reconsent**

If you select any of these study statuses under Section I of the continuing review form, you must make the following updates, as appropriate.

☐ Ensure the cost, payment, and injury statements in the informed consent statement(s) (ICS) meet the criteria outlined in the ICS checklist (items 8.a, 8.b, and 8.c.). This can be found at: http://www.iupui.edu/%7Eresgrad/irbpacket/ic-checklist.rtf.

☐ In the ICS, include the following statement to list Research Compliance Administration as an alternate contact when the PI cannot be reached or for problems, concerns, questions, etc. (***NOTE: This statement is not intended to replace any emergency contact***):

"If you cannot reach the researcher during regular business hours (i.e. 8:00AM-5:00PM), please call the IUPUI/Clarian Research Compliance Administration office at 317/278-3458 or 800/696-2949."

☐ In the ICS, include the following statement to list Research Compliance Administration as a contact for subjects to discuss problems, concerns and questions, obtain information, offer input, or to find out about their rights:

"For questions about your rights as a research participant or to discuss problems, complaints or concerns about a research study, or to obtain information, or offer input, contact the IUPUI/Clarian Research Compliance Administration office at 317/278-3458 or 800/696-2949."

☐ In the ICS, list all appropriate organizations/agencies, specifically the Office for Human Research Protections (OHRP), who may have access to or inspect subjects' medical and/or research records. See ICS template for additional information (http://www.iupui.edu/%7Eresgrad/irbpacket/ic-template.rtf).

☐ If the investigator wishes to continue to follow subjects' health and collect clinical data from subjects' medical records after they have withdrawn from the study, submit an addendum to the current informed consent or develop a separate informed consent to allow subjects to "opt-in" or "opt-out" of this continued data collection at the time they withdraw from the study. (Reference December 2004 R&SP Communicator, http://www.iupui.edu/%7Erspcommu/2004/nl-december-04.htm).

SPECIAL CIRCUMSTANCES: Only for research studies that are actively enrolling certain subject populations.

☐ **STUDIES INVOLVING CHILDREN.** As a result of a new policy instituted by the IRB Executive Committee with regard to obtaining assent from children to enter a clinical trial, please submit an assent document for children aged 7 to 17 if your study is still actively enrolling children and does not currently include an assent document.

☐ **VA STUDIES.** In an effort to comply with VA regulations, please submit the required VA-specific informed consent form 10-1086 if you are actively enrolling subjects at the VA. For studies that do not currently have this informed consent in place, please submit one for review and approval at this time.

SPECIAL CIRCUMSTANCES: Only for ONGOING studies and studies that are **ONGOING, Permanently closed to subject enrollment that still include ACTIVE subjects.**

☐ Submit a complete protocol if the IRB does not have a current, complete protocol. For example, if a study amendment that affected the protocol was approved since the last IRB review and the complete, revised protocol was not submitted with that amendment (e.g. only updated pages of the protocol were submitted), a current and complete protocol must be submitted. Please see Section VI of the continuing review form for additional information.

	Since beginning of study	Number of subjects **CONSENTED/ENROLLED**	
		Number of subjects who **FAILED SCREENING** (e.g. found ineligible to participate)	**n/a**
		Number of subjects who have **WITHDRAWN** from the study	**n/a**
	Number of **ACTIVE** subjects		**n/a**
	Number of subjects who have **COMPLETED** the study		**n/a**

2. WITHDRAWAL

Have any subjects withdrawn from the study since the last IRB review? N/A-secondary data analysis.

☒ No

☐ Yes, state the reasons for them:_____

3. JUSTIFICATION FOR STUDY CONTINUATION – Only complete if the study remains open to subject enrollment

Have subjects accrued in the study since the last IRB review?

☐ Yes

☒ No, justify study continuation: **Study is retrospective data analysis for dissertation project.**

4. Check if any accrued subjects are:

☐ Children ☐ Pregnant Women and Fetuses
☐ Prisoners ☐ Economically/Educationally Disadvantaged
☐ Cognitively Impaired ☐ Students

If any of the above populations have been accrued, was this previously approved by the IRB?

☐ No. Submit an amendment to the study to request the inclusion of the group of subjects checked above.

☐ Yes.

SECTION III: ETHNIC/RACIAL REPORTING REQUIRED FOR FEDERALLY-SPONSORED STUDIES

Indicate the ethnic and racial categories for subjects accrued to date for all federally-sponsored (e.g. NIH, VA, CDC, etc.) studies or studies conducted at the VA or using VA subjects. The numbers should reflect subjects on-site.

No subjects were recruited for this study since it is a retrospective data analysis for a dissertation project.

SUBJECT ACCRUAL				
Ethnic Category	**Sex/Gender**			**Total**
	Females	**Males**	**Unknown or Not Reported**	**n/a retrospective data analysis**
Hispanic or Latino				
Not Hispanic or Latino				
Unknown (Individuals Not Reporting Ethnicity)				
Ethnic Category Total of All Subjects*				
Racial Categories				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or Not Reported				
Racial Categories Total of All Subjects*				

If ETHNIC and RACIAL category totals are not equal, please explain: _____

Have there been any unexpected difficulties accruing subjects in a particular category (including children and women)?

☒ No.
☐ Yes. Please explain: _____

FOR VA STUDIES ONLY (i.e. all studies conducted at the VA or using VA patients). For the total number of subjects noted in the table above, include the total number in the following categories (state "0" if the there have been none enrolled):

Children:
Cognitively Impaired:
Economically/Educationally Disadvantaged:
Pregnant Women and Fetuses:
Prisoners:
Students:

SECTION IV: SUMMARY OF EVENTS

IV.A. Did any events that require prompt reporting to the IRB occur **since the last IRB review** (Refer to 4.5 of the Unanticipated Problems Involving Risks to Subjects or Others and Noncompliance SOP for a list of events that require prompt reporting to the IRB, hereafter referred to as THE LIST)?:
- ☒ No.
- ☐ Yes. Were these events reported previously to both the IRB and VA, if applicable?
  - ☐ No. Please explain: _____
  - ☐ Yes. Provide a SUMMARY of these events: _____
    - ☐ Check here if the SUMMARY is attached.

IV.B. Provide a summary of all other events not on THE LIST (e.g. adverse events, protocol deviations, problems, complaints, etc.) that occurred **on-site since the last IRB review** (The summary should include events not on THE LIST that represent an increase in severity or frequency over what is known or expected): _____
- ☐ Check here if SUMMARY is attached.
- ☒ Check here if no other events occurred

IV.C. Is there a Data Safety Monitoring Board for this study?
- ☒ No.
- ☐ Yes. Provide the most recent monitoring report or explain: _____

IV.D. Based on the above information, do you feel the validity of the data is affected?
- ☒ No.
- ☐ Yes. Explain:

IV.E. Based on the above information, do you feel there is a significant increase in risk to subjects or others or in the frequency or severity of adverse events, protocol deviations, problems, complaints, etc. since the last IRB review?
- ☒ No.
- ☐ Yes. Explain: _____

SECTION V: SUMMARY

V.A. Provide a summary of the study's progress (e.g. information about study results or trends):

Data analysis for this project is completed. The student is now working on the write up of results.

V.B. Provide a summary of actual benefits experienced by accrued subjects (on-site): _____
V.B.1. If unknown or not applicable, explain: No benefits for study since it is a secondary data analysis._____

V.C. If any recent literature has been published or presented by you or others since the last IRB review, has it demonstrated a significant impact on the conduct of the study or the well-being of subjects?
- ☒ N/A. There has not been any recent literature published or presented since the last IRB review.
- ☐ No.

☐ Yes. Attach a copy or explain: _____

V.D. Have there been any audits from a federal agency conducted since the last IRB review that identified unanticipated problems involving risks to subjects or others?
☒ No.
☐ Yes. Attach the report(s).

V.E. Are you collaborating with any UNAFFILIATED investigators?
☒ No.
☐ Yes. Identify the investigator(s) and explain their role(s) in the study: _____

Is an Unaffiliated Investigator Agreement in place?
☐ No. Submit an amendment to add one, or explain why one is not needed: ____
☐ Yes.

V.F. Have any conflicts of interest arisen since the last IRB review, which have not been previously reported to the IRB and (if applicable) to the VA Financial Conflict of Interest committee (using VA Form 10-1313-14)?
☒ No.
☐ Yes. Explain:_____

V.G. Do you believe the risk:benefit ratio has changed based on all of the information provided on this form and any attachments?
☒ No.
☐ Yes. Explain:_____

SECTION VI: ATTACHMENTS

☐ Informed Consent
☒ Summary Safeguard Statement
☐ Authorization
☐ Recruitment Materials
☐ DSMB report
☐ Publications
☐ National Summary Reports
☐ Audit Reports
☒ Protocol
☐ Other, Description:

REQUIRED ATTACHMENTS:

STUDY STATUS	SSS	Recruitment Checklist	ICS/ Assent	AUTH	Advertise-ments	PROTOCOL
ONGOING	X[1]	X	X	X	X	X[4]
ONGOING, Permanently closed to subject enrollment	X[2]		X[3]	X[3]		X[4]
WILL NOT BE INITIATED						
COMPLETED						
CLOSED PRIOR TO COMPLETION						

1 Must submit version 06/05 or later of the summary safeguard statement.

2 Can submit any version of the summary safeguard statement as long as the information provided within is up-to-date and accurate.

3 Only need to submit if subjects will be reconsented and/or reauthorized (ONGOING – Permanently closed to subject enrollment status only).

4 Must submit a copy of the current COMPLETE protocol (which incorporates all amendments) for all ONGOING studies and studies that are ONGOING, Permanently closed to subject enrollment, which still include ACTIVE subjects if the IRB does not have a current, complete protocol. For example, if a study amendment that affected the protocol was approved since the last IRB review and the complete, revised protocol was not submitted with that amendment (e.g. only updated pages of the protocol were submitted), a current and complete protocol must be submitted with the continuing review.

5 The following must be submitted, unless previously reported to the IRB:
- Publications (any publications or abstracts derived from the study since the last IRB review), if applicable. (See V.C. of the form)
- National Summary Reports (findings from multi-center study group) since the last IRB review, if applicable.
- Audit Reports, if applicable (See V.D. of the form)
- Interim Findings

- Summaries (e.g. events that require prompt reporting to the IRB, as referenced in IV.A of this form).

Your signature certifies that this study has been and will continue to be conducted in full compliance with the IRB-approved protocol, HHS/FDA regulations and the IUPUI Clarian policies governing human subject research. You also certify that the information contained on or with this form is accurate.

Signature of Principal Investigator: email_____Date: 12/10/2007

SECTION VII: IRB APPROVAL

***** For Office Use Only *****

Type of review: ☐ Full Board

☒ Expedited, Category: 7

IRB Reviewer:

☐ Check here to confirm that the most recent informed consent statement has been reviewed and no additional information needs to be provided to subjects based on any new findings.

STATUS OF STUDY: (RCA staff to indicate)

☐ **ONGOING**: This continuing review has been reviewed and approved by the IUPUI/ Clarian Institutional Review Board (IRB). Based on the criteria for determining the frequency of continuing review and the level of risk, this study will expire on: DEC 21 2008. If the study is not re-approved prior to that date all research activities must cease on that date, including enrollment of new subjects, intervention on current participants, and analysis of identified data.

☐ **COMPLETED/CLOSED:** This close-out report has been reviewed and accepted by the IUPUI/Clarian Institutional Review Board (IRB).

Authorized IRB Signature:_____IRB Approval Date: 12-21-07

Recorded in the Minutes of: FEB 01 2008

APPENDIX G

Data Cleaning Procedures

Variable	Measure	Items Missing	Decision
Sleep	PSQI	38 out of 8856 items 0.43% missing	Mean substitution of hours of sleep by a narrow mean of group (BCS, WWBC) and race or age. For Q14-since it is an 'other' category assuming no was imputed.
Type of cancer treatment	MRAF [1]	No radiation treatment information for ACS women	Radiation therapy will not be included in treatment items and is listed as a limitation of the study.
Anxiety	STAI	All AA=160 and ACS=7 (questionnaires not answered) Total missing items=305 out of 13000 2.35% missing for those that completed.	STAI measure was eliminated due to Multicolinearity with the CES-D. CES-D scores were entered into a correlation matrix with state and trait STAI scores since anxiety and depression are typically highly correlated. A correlation near or above .7 would mean the two questionnaires are highly related (Tabachnick & Fidell, 2001). The correlation for State/CES-D 0.67 and Trait/CES-D 0.75. This would mean that the STAI and CES-D are correlated with possible redundancy in variables (depression and anxiety).
Distress r/t life event	IES-revised	98 out of 9840 1% missing	Mean substitution by group was performed for missing values. Scores were averaged to produce scores for items 13 and 19 were inadvertently not included in the measure. Scales and total were recalculated.
SES	PCQ WI	21 single-items out of 492 4.26% missing	Mean substitution imputed based on mean income by group and race.

Variable	Measure	Items Missing	Decision
Long-term side effects	SER[1]	30 items out of 9852 for BCS 0.30% missing	Imputed response of 0 meaning 'no' for responses for missing values since using a mean might make the false assumption that the symptom was present without severity rating being present.
Physical functioning	PF-10	4 items total of 4920 0.06% missing	No action needed. Mean imputation did not change scores included in dataset.
Cancer related distress	CARS [1]	3 items total of 984 0.30% missing	Mean responses were 1 for missing items. The mean changed only by .01 from current scores provided by parent dataset.
Depression	CES-D	85 out of 9840 items 0.86% missing	Used mean imputation from SPSS which places a mean of that item into missing values. When performed, the mean scores did not significantly change.
Race	PCQ	0 out of 492	Those that listed multiple races or no race were categorized as "other".
Menopausal status	MGHQ	0 out of 492 after missing values entered	New variable created based on question 2 of questionnaire. For missing values, questions regarding gynecology history were evaluated for any indication of hysterectomy, oophorectomy, or time menstrual cycles stopped, if a date was listed status was changed in this variable to reflect pre-post menopause status. This process identified the status of the 6 that were missing. Two decisions were made based on age-below 45 the women were considered pre-menopausal because they responded 'no' to surgery or other indicators of being post-menopausal (e.g., hot flashes).

Variable	Measure	Items Missing	Decision
Co-morbidities (number of)	MHQ	0 out of 492	The list of co morbidities was grouped into categorical #'s. These questions had only a 'yes' response in the questionnaire thus if blank-assumption is that it is a 'no' response.
Post-menopausal Hot flashes Yes/No	MGHQ	0 out of 492	Created a variable for hot flashes yes/no based on item 12 in MGHQ. No missing values found.
Companion/bed partner	PSQI	0 out of 492	None-no missing values. Also verified with a different question in database regarding marital status and partnered yes/no. This question from PSQI captures those that are partner and not sleeping in separate rooms.

REFERENCES

Akerstedt, T., Hume, K., Minors, D., & Waterhouse, J. (1994). The subjective meaning of good sleep, an intraindividual approach using the Karolinska Sleep Diary. *Perception & Motor Skills, 79*(1), 287-296.

American Cancer Society. (2008). *Cancer Facts and Figures 2008* (report No. 500808). Atlanta: American Cancer Society.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders: DSM-IV* (4th ed.). Washington, DC: American Psychiatric Association.

American Sleep Disorders Association. (1994). *International classification of sleep disorders: Revised*. Rochester: American Sleep Disorders Association.

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. P. (2003). The role of actigraphy in the study of sleep and circadian rhythms. *Sleep, 26*(3), 342-392.

Ancoli-Israel, S., Liu, L., Marler, M. R., Parker, B. A., Jones, V., Sadler, G. R., et al. (2005). Fatigue, sleep, and circadian rhythms prior to chemotherapy for breast cancer. *Supportive Care in Cancer, 14*(3), 201-209.

Ancoli-Israel, S., Moore, P. J., & Jones, V. (2001). The relationship between fatigue and sleep in cancer patients: A review. *European Journal of Cancer Care (English Language Edition), 10*(4), 245-255.

Anderson, K. O., Getto, C. J., Mendoza, T. R., Palmer, S. N., Wang, X. S., Reyes-Gibby, C. C., et al. (2003). Fatigue and sleep disturbance in patients with cancer, patients with clinical depression, and community-dwelling adults. *Journal of Pain and Symptom Management, 25*(4), 307-318.

Andrykowski, M. A., Carpenter, J. S., Greiner, C. B., Altmaier, E. M., Burish, T. G., Antin, J. H., et al. (1997). Energy level and sleep quality following bone marrow transplantation. *Bone Marrow Transplantation, 20*(8), 669-679.

Andrykowski, M. A., Curran, S. L., & Lightner, R. (1998). Off-treatment fatigue in breast cancer survivors: A controlled comparison. *Journal of Behavioral Medicine, 21*(1), 1-18.

Anker, G. B., Lonning, P. E., Aakvaag, A., & Lien, E. A. (1998). Thyroid function in postmenopausal breast cancer patients treated with tamoxifen. *Scandinavian Journal of Clinical and Laboratory Investigation, 58*(2), 103-107.

Aschoff, J. (1965). Circadian Rhythms in Man. *Science, 148*(3676), 1427-1432.

Aserinsky, E., & Kleitman, N. (1953). Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. *Science, 118*(3062), 273-274.

Baker, A., Simpson, S., & Dawson, D. (1997). Sleep disruption and mood changes associated with menopause. *Journal of Psychosomatic Research, 43*(4), 359-369.

Bastien, C. H., Vallieres, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine, 2*(4), 297-307.

Beck, S. L., Schwartz, A. L., Towsley, G., Dudley, W., & Barsevick, A. (2004). Psychometric evaluation of the Pittsburgh Sleep Quality Index in cancer patients. *Journal of Pain and Symptom Management, 27*(2), 140-148.

Benca, R. M. (2005). Diagnosis and treatment of chronic insomnia: A review. *Psychiatric Services, 56*(3), 332-343.

Berger, A. M. (1998). Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum, 25*(1), 51-62.

Berger, A. M., & Farr, L. (1999). The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncology Nursing Forum, 26*(10), 1663-1671.

Berger, A. M., & Higginbotham, P. (2000). Correlates of fatigue during and following adjuvant breast cancer chemotherapy: A pilot study. *Oncology Nursing Forum, 27*(9), 1443-1448.

Berger, A. M., Parker, K. P., Young-McCaughan, S., Mallory, G. A., Barsevick, A. M., Beck, S. L., et al. (2005). Sleep wake disturbances in people with cancer and their caregivers: State of the science. *Oncology Nursing Forum, 32*(6), E98-126.

Berger, A. M., VonEssen, S., Khun, B. R., Piper, B. F., Farr, L., Agrawal, S., et al. (2002). Feasibility of a sleep intervention during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum, 29*(10), 1431-1441.

Berger, A. M., VonEssen, S., Kuhn, B. R., Piper, B. F., Agrawal, S., Lynch, J. C., et al. (2003). Adherence, sleep, and fatigue outcomes after adjuvant breast cancer chemotherapy: Results of a feasibility intervention study. *Oncology Nursing Forum, 30*(3), 513-522.

Berger, A. M., & Walker, S. N. (2001). An explanatory model of fatigue in women receiving adjuvant breast cancer chemotherapy. *Nursing Research, 50*(1), 42-52.

Berkman, L. F., Berkman, C. S., Kasl, S., Freeman, D. H., Jr., Leo, L., Ostfeld, A. M., et al. (1986). Depressive symptoms in relation to physical health and functioning in the elderly. *American Journal of Epidemiology, 124*(3), 372-388.

Bleiker, E. M., Pouwer, F., van der Ploeg, H. M., Leer, J. W., & Ader, H. J. (2000). Psychological distress two years after diagnosis of breast cancer: Frequency and prediction. *Patient Education and Counseling, 40*(3), 209-217.

Blesch, K. S., Paice, J. A., Wickham, R., Harte, N., Schnoor, D. K., Purl, S., et al. (1991). Correlates of fatigue in people with breast or lung cancer. *Oncology Nursing Forum, 18*(1), 81-87.

Borbely, A. A. (1982). A two process model of sleep regulation. *Human Neurobiology, 1*(3), 195-204.

Borbely, A. A., & Achermann, P. (1992). Concepts and models of sleep regulation: An overview. *Journal of Sleep Research, 1*(2), 63-79.

Borbely, A. A., & Achermann, P. (1999). Sleep homeostasis and models of sleep regulation. *Journal of Biological Rhythms, 14*(6), 557-568.

Bower, J. E., Ganz, P. A., Desmond, K. A., Rowland, J. H., Meyerowitz, B. E., & Belin, T. R. (2000). Fatigue in breast cancer survivors: Occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology, 18*(4), 743-753.

Bowman, T. J. (2003). Normal sleep patterns. In T. J. Bowman (Ed.), *Review of Sleep Medicine* (pp. 166-201). Boston: Butterworth & Heinemann.

Bowman, T. J., & Moshenin, V. (2003). Synopsis of sleep. In T. J. Bowman (Ed.), *Review of Sleep Medicine* (pp. 3-18). Boston: Butterworth & Heinemann.

Broeckel, J. A., Jacobsen, P. B., Horton, J., Balducci, L., & Lyman, G. H. (1998). Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology, 16*(5), 1689-1696.

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

Buysse, D. J., Reynolds, C. F. r., Monk, T. H., Hoch, C. C., Yeager, A. L., & Kupfer, D. J. (1991). Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). *Sleep, 14*(4), 331-338.

Cappiello, M., Cunningham, R. S., Knobf, M. T., & Erdos, D. (2007). Breast cancer survivors: Information and support after treatment. *Clinical Nursing Research, 16*(4), 278-293; discussion 294-301.

Carpenter, J. S. (2000). Hot flashes and their management in breast cancer. *Seminars in Oncology Nursing, 16*(3), 214-225.

Carpenter, J. S., & Andrykowski, M. A. (1998). Psychometric evaluation of the Pittsburgh Sleep Quality Index. *Journal of Psychosomatic Research, 45*(1), 5-13.

Carpenter, J. S., & Andrykowski, M. A. (1999). Menopausal symptoms in breast cancer survivors. *Oncology Nursing Forum, 26*(8), 1311-1317.

Carpenter, J. S., Andrykowski, M. A., Cordova, M., Cunningham, L., Studts, J., McGrath, P., et al. (1998). Hot flashes in postmenopausal women treated for breast carcinoma: Prevalence, severity, correlates, management, and relation to quality of life. *Cancer, 82*(9), 1682-1691.

Carpenter, J. S., Andrykowski, M. A., Cordova, M. J., Cunningham, L. L., & Studts, J. L. (1999). Do participants' reports of symptom prevalence or severity vary by interviewer gender? *Nursing Research, 48*(5), 276-279.

Carpenter, J. S., Elam, J., Ridner, S., Carney, P., Cherry, G., & Cucullu, H. (2004). Sleep, fatigue, and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. *Oncology Nursing Forum, 31*(3), 591-5598.

Carpenter, J. S., Gautam, S., Freedman, R. R., & Andrykowski, M. (2001). Circadian rhythm of objectively recorded hot flashes in postmenopausal breast cancer survivors. *Menopause, 8*(3), 181-188.

Carpenter, J. S., Johnson, D., Wagner, L., & Andrykowski, M. A. (2002). Hot flashes and related outcomes in breast cancer survivors and matched comparison women. *Oncology Nursing Forum, 29*(3), E16-25.

Carpenter, J. S., Neal, J. G., Payne, J. K., Kimmick, G., & Storniolo, A. M. (2007). Cognitive-behavioral intervention for hot flashes. *Oncology Nursing Forum, 34*(1), E1-8.

Cermakian, N., & Boivin, D. B. (2003). A molecular perspective of human circadian rhythm disorders. *Brain Research Reviews, 42*(3), 204-220.

Cheek, R. E., Shaver, J. L., & Lentz, M. J. (2004). Lifestyle practices and nocturnal sleep in midlife women with and without insomnia. *Biological Research for Nursing, 6*(1), 46-58.

Chen, S. T., Choo, K. B., Hou, M. F., Yeh, K. T., Kuo, S. J., & Chang, J. G. (2005). Deregulated expression of the PER1, PER2 and PER3 genes in breast cancers. *Carcinogenesis, 26*(7), 1241-1246.

Chernecky, C. C., & Berger, B. J. (2004). *Laboratory tests & diagnostic procedures* (4th ed.). Philadelphia: Saunders.

Clark, A. J., Flowers, J., Boots, L., & Shettar, S. (1995). Sleep disturbance in mid-life women. *Journal of Advanced Nursing, 22*(3), 562-568.

Clark, J., Cunningham, M., McMillan, S., Vena, C., & Parker, K. (2004). Continuing education: Sleep-wake disturbances in people with cancer part II: Evaluating the evidence for clinical decision making. *Oncology Nursing Forum, 31*(4), 747-771.

Claustrat, B., Brun, J., & Chazot, G. (2005). The basic physiology and pathophysiology of melatonin. *Sleep Medicine Reviews, 9*(1), 11-24.

Cleeland, C. S. (1993). Strategies for improving cancer pain management. *Journal of Pain and Symptom Management, 8*(6), 361-364.

Cleeland, C. S., Gonin, R., Hatfield, A. K., Edmonson, J. H., Blum, R. H., Stewart, J. A., et al. (1994). Pain and its treatment in outpatients with metastatic cancer. *New England Journal of Medicine, 330*(9), 592-596.

Comstock, G. W., & Helsing, K. J. (1976). Symptoms of depression in two communities. *Psychological Medicine, 6*(4), 551-563.

Couzi, R. J., Helzlsouer, K. J., & Fetting, J. H. (1995). Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. *Journal of Clinical Oncology, 13*(11), 2737-2744.

Crandall, C., Petersen, L., Ganz, P. A., & Greendale, G. A. (2004). Association of breast cancer and its therapy with menopause-related symptoms. *Menopause, 11*(5), 519-530.

Davidson, J. R., MacLean, A. W., Brundage, M. D., & Schulze, K. (2002). Sleep disturbance in cancer patients. *Social Science & Medicine, 54*(9), 1309-1321.

Davidson, J. R., Waisberg, J. L., Brundage, M. D., & MacLean, A. W. (2001). Nonpharmacologic group treatment of insomnia: A preliminary study with cancer survivors. *Psycho-Oncology, 10*(5), 389-397.

de Souza, L., Benedito-Silva, A. A., Pires, M. L., Poyares, D., Tufik, S., & Calil, H. M. (2003). Further validation of actigraphy for sleep studies. *Sleep, 26*(1), 81-85.

Deimling, G. T., Kahana, B., Bowman, K. F., & Schaefer, M. L. (2002). Cancer survivorship and psychological distress in later life. *Psycho-Oncology, 11*(6), 479-494.

Dement, W. C., & Vaughan, C. C. (2000). *The promise of sleep: A pioneer in sleep medicine explores the vital connection between health, happiness, and a good night's sleep*. New York: Dell Trade Paperback.

Dogan, O., Ertekin, S., & Dogan, S. (2005). Sleep quality in hospitalized patients. *Journal of Clinical Nursing, 14*(1), 107-113.

Donovan, M. I., & Dillon, P. (1987). Incidence and characteristics of pain in a sample of hospitalized cancer patients. *Cancer Nursing, 10*(2), 85-92.

Dow, K. H. (Ed.). (2004). *Contemporary issues in breast cancer: A nursing perspective* (2nd ed.). Sudbury: Jones and Bartlett.

Dow, K. H., Ferrell, B. R., Leigh, S., Ly, J., & Gulasekaram, P. (1996). An evaluation of the quality of life among long-term survivors of breast cancer. *Breast Cancer Research & Treatment, 39*(3), 261-273.

Dzaja, A., Arber, S., Hislop, J., Kerkhofs, M., Kopp, C., Pollmacher, T., et al. (2005). Women's sleep in health and disease. *Journal of Psychiatric Research, 39*(1), 55-76.

Elam, J. L., & Carpenter, J. S. (2004a). Evaluation of subjective sleep for breast cancer survivors experiencing hot flashes. Poster session presented at the annual meeting of the Midwest Nursing Research Society. Cincinnati, OH.

Elam, J. L., & Carpenter, J. S. (2004b). Results of Pittsburgh Sleep Quality Index parameters for female beast cancer survivors seeking treatment for hot flashes. Poster session presented at the annual research meeting of the Sigma Theta Tau International Nursing Society. Dublin, IR.

Elam, J. L., & Carpenter, J. S. (2005). Relationships among objective sleep parameters, objective hot flashes, and subjective hot flashes in breast cancer survivors. Poster session presented at the National Oncology Nursing Society Research Conference. Ft. Lauderdale, FL.

Empson, J. A., & Purdie, D. W. (1999). Effects of sex steroids on sleep. *Annals of Medicine, 31*(2), 141-145.

Engstrom, C. A., Strohl, R. A., Rose, L., Lewandowski, L., & Stefanek, M. E. (1999). Sleep alterations in cancer patients. *Cancer Nursing, 22*(2), 143-148.

Eriguchi, M., Levi, F., Hisa, T., Yanagie, H., Nonaka, Y., & Takeda, Y. (2003). Chronotherapy for cancer. *Biomedicine and Pharmacotherapy, 57*(Suppl. 1), 92-95.

Espie, C. A. (2002). Insomnia: Conceptual issues in the development, persistence, and treatment of sleep disorder in adults. *Annual Review of Psychology, 53*(1), 215-243.

Faruque, S., Bowman, T. J., & Sisson, J. H. (2003). Sleep physiology. In T. J. Bowman (Ed.), *Review of Sleep Medicine* (pp. 42-56). Boston: Butterworth & Heinemann.

Fava, M. (2004). Daytime sleepiness and insomnia as correlates of depression. *Journal of Clinical Psychiatry, 65*(Suppl. 16), 27-32.

Ferrell, B. R., Grant, M., Funk, B., Garcia, N., Otis-Green, S., & Schaffner, M. L. (1996). Quality of life in breast cancer. *Cancer Practice, 4*(6), 331-340.

Field, A. P. (2005). *Discovering statistics using SPSS* (2nd ed.). Thousand Oaks: SAGE.

Filipski, E., King, V. M., Li, X., Granda, T. G., Mormont, M. C., Liu, X., et al. (2002). Host circadian clock as a control point in tumor progression. *Journal of the National Cancer Institute, 94*(9), 690-697.

Folstein, M. F., & Whitehouse, P. J. (1983). Cognitive impairment of Alzheimer disease. *Neurobehavioral Toxicology and Teratology, 5*(6), 631-634.

Fortner, B. V., Stepanski, E. J., Wang, S. C., Kasprowicz, S., & Durrence, H. H. (2002). Sleep and quality of life in breast cancer patients. *Journal of Pain and Symptom Management, 24*(5), 471-480.

Freedman, R. R., & Roehrs, T. A. (2007). Sleep disturbance in menopause. *Menopause, 14*(5), 826-829.

Fry, J. M. (1987). Sleep disorders. *Medical Clinics of North America, 71*(1), 95-110.

Ganz, P. A. (2005). Breast cancer, menopause, and long-term survivorship: Critical issues for the 21st century. *American Journal of Medicine, 118*(12 Suppl. 2), 136-141.

Ganz, P. A., Desmond, K. A., Leedham, B., Rowland, J. H., Meyerowitz, B. E., & Belin, T. R. (2002). Quality of life in long-term, disease-free survivors of breast cancer: A follow-up study. *Journal of the National Cancer Institute, 94*(1), 39-49.

Gellis, L. A., Lichstein, K. L., Scarinci, I. C., Durrence, H. H., Taylor, D. J., Bush, A. J., et al. (2005). Socioeconomic status and insomnia. *Journal of Abnormal Psychology, 114*(1), 111-118.

Gentili, A., Weiner, D. K., Kuchibhatil, M., & Edinger, J. D. (1997). Factors that disturb sleep in nursing home residents. *Aging, 9*(3), 207-213.

Gentili, A., Weiner, D. K., Kuchibhatla, M., & Edinger, J. D. (1995). Test-retest reliability of the Pittsburgh Sleep Quality Index in nursing home residents. *Journal of the American Geriatrics Society, 43*(11), 1317-1318.

Giani, C., Fierabracci, P., Bonacci, R., Gigliotti, A., Campani, D., De Negri, F., et al. (1996). Relationship between breast cancer and thyroid disease: Relevance of autoimmune thyroid disorders in breast malignancy. *Journal of Clinical Endocrinology and Metabolism, 81*(3), 990-994.

Giesler, R. B., Given, B., Given, C. W., Rawl, S., Monahan, P., Burns, D., et al. (2005). Improving the quality of life of patients with prostate carcinoma: A randomized trial testing the efficacy of a nurse-driven intervention. *Cancer, 104*(4), 752-762.

Graydon, J. E., Bubela, N., Irvine, D., & Vincent, L. (1995). Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nursing, 18*(1), 23-28.

Grimm, L. G., & Yarnold, P. R. (2000). *Reading and understanding more multivariate statistics* (1st ed.). Washington, DC: American Psychological Association.

Guyton, A. C., & Hall, J. E. (1997). *Human physiology and mechanisms of disease* (6th ed.). Philadelphia: Saunders.

Haley, S. M., McHorney, C. A., & Ware, J. E., Jr. (1994). Evaluation of the MOS SF-36 physical functioning scale (PF-10): I. Unidimensionality and reproducibility of the Rasch item scale. *Journal of Clinical Epidemiology, 47*(6), 671-684.

Hall, M., Baum, A., Buysse, D. J., Prigerson, H. G., Kupfer, D. J., & Reynolds, C. F., 3rd. (1998). Sleep as a mediator of the stress-immune relationship. *Psychosomatic Medicine, 60*(1), 48-51.

Hall, M., Bromberger, J., & Matthews, K. (1999). Socioeconomic status as a correlate of sleep in African-American and Caucasian women. *Annals of the New York Academy of Sciences, 896*(1), 427-430.

Hall, M., Vasko, R., Buysse, D., Ombao, H., Chen, Q., Cashmere, J. D., et al. (2004). Acute stress affects heart rate variability during sleep. *Psychosomatic Medicine, 66*(1), 56-62.

Hann, D., Winter, K., & Jacobsen, P. (1999). Measurement of depressive symptoms in cancer patients: Evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *Journal of Psychosomatic Research, 46*(5), 437-443.

Harvey, A. G. (2002). A cognitive model of insomnia. *Behavior Research and Therapy, 40*(8), 869-893.

Harvey, K. J., & Espie, C. A. (2004). Development and preliminary validation of the Glasgow Content of Thoughts Inventory (GCTI): A new measure for the assessment of pre-sleep cognitive activity. *British Journal of Clinical Psychology, 43*(4), 409-420.

Hauri, P. J., & Wisbey, J. (1992). Wrist actigraphy in insomnia. *Sleep, 15*(4), 293-301.

Hicks, R. A., Lucero-Gorman, K., Bautista, J., & Hicks, G. J. (1999). Ethnicity, sleep hygiene knowledge, and sleep hygiene practices. *Perceptual and Motor Skills, 88*(3 Pt 2), 1095-1096.

Higginson, I. J., & Hearn, J. (1997). A multicenter evaluation of cancer pain control by palliative care teams. *Journal of Pain and Symptom Management, 14*(1), 29-35.

Holbrook, A. M., Crowther, R., Lotter, A., Cheng, C., & King, D. (2000a). The diagnosis and management of insomnia in clinical practice: A practical evidence-based approach. *Canadian Medical Association Journal, 162*(2), 216-220.

Holbrook, A. M., Crowther, R., Lotter, A., Cheng, C., & King, D. (2000b). Meta-analysis of benzodiazepine use in the treatment of insomnia. *Canadian Medical Association Journal, 162*(2), 225-233.

Horowitz, M., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: A measure of subjective stress. *Psychosomatic Medicine, 41*(3), 209-218.

Hosmer, D. W., & Lemeshow, S. (2000). *Applied logistic regression* (2nd ed.). New York: Wiley.

Hunter, M. S., Grunfeld, E. A., Mittal, S., Sikka, P., Ramirez, A. J., Fentiman, I., et al. (2004). Menopausal symptoms in women with breast cancer: Prevalence and treatment preferences. *Psycho-Oncology, 13*(11), 769-778.

Jean-Louis, G., Kripke, D. F., Assmus, J. D., & Langer, R. D. (2000). Sleep-wake patterns among postmenopausal women: A 24-hour unattended polysomnographic study. *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 55*(3), M120-123.

Jefferson, C. D., Drake, C. L., Scofield, H. M., Myers, E., McClure, T., Roehrs, T., et al. (2005). Sleep hygiene practices in a population-based sample of insomniacs. *Sleep, 28*(5), 611-615.

Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., Murray, T., et al. (2008). Cancer statistics, 2008. *CA: A Cancer Journal for Clinicians, 58*(2), 71-96.

Jones, C. R., & Czajkowski, L. (2000). Evaluation and management of insomnia in menopause. *Clinical Obstetrics and Gynecology, 43*(1), 184-197.

Keenan, S. A. (2003). Polysomnographic technique: An overview. In T. J. Bowman (Ed.), *Review of Sleep Medicine* (pp. 107-132). Boston: Butterworth & Heinemann.

Kerner, J., Rimer, B., & Emmons, K. (2005). Dissemination research and research dissemination: How can we close the gap? *Health Psychology, 24*(5), 443-446.

Kloss, J. D., Tweedy, K., & Gilrain, K. (2004). Psychological factors associated with sleep disturbance among perimenopausal women. *Behavioral Sleep Medicine, 2*(4), 177-190.

Konopka, R. J., & Benzer, S. (1971). Clock mutants of Drosophila melanogaster. *Proceedings of the National Academy of Sciences of the United States of America, 68*(9), 2112-2116.

Koopman, C., Nouriani, B., Erickson, V., Anupindi, R., Butler, L. D., Bachmann, M. H., et al. (2002). Sleep disturbances in women with metastatic breast cancer. *Breast Journal, 8*(6), 362-370.

Kopelman, P. G., Apps, M. C., Cope, T., & Empey, D. W. (1985). The influence of menstrual status, body weight and hypothalamic function on nocturnal respiration in women. *Journal of the Royal College of Physicians of London, 19*(4), 243-247.

Krauchi, K., & Wirz-Justice, A. (2001). Circadian clues to sleep onset mechanisms. *Neuropsychopharmacology, 25*(Suppl. 5), S92-96.

Kravitz, H. M., Ganz, P. A., Bromberger, J., Powell, L. H., Sutton-Tyrrell, K., & Meyer, P. M. (2003). Sleep difficulty in women at midlife: A community survey of sleep and the menopausal transition. *Menopause, 10*(1), 19-28.

Kushida, C. A., Chang, A., Gadkary, C., Guilleminault, C., Carrillo, O., & Dement, W. C. (2001). Comparison of actigraphic, polysomnographic, and subjective assessment of sleep parameters in sleep-disordered patients. *Sleep Medicine, 2*(5), 389-396.

Lacks, P., & Rotert, M. (1986). Knowledge and practice of sleep hygiene techniques in insomniacs and good sleepers. *Behavior Research and Therapy, 24*(3), 365-368.

Lavie, P. (2001). Sleep-wake as a biological rhythm. *Annual Review of Psychology, 52*(1), 277-303.

Lee, K., Cho, M., Miaskowski, C., & Dodd, M. (2004). Impaired sleep and rhythms in persons with cancer. *Sleep Medicine Review, 8*(3), 199-212.

Lee-Chiong, T. L., Jr. (2004). Sleep and sleep disorders: An overview. *Medical Clinics of North America, 88*(3), xi-xiv.

Leibenluft, E. (1993). Do gonadal steroids regulate circadian rhythms in humans? *Journal of Affective Disorders, 29*(2-3), 175-181.

Lin, T. L., Ng, S. C., Chen, Y. C., Hu, S. W., & Chen, G. D. (2005). What affects the occurrence of nocturia more: Menopause or age? *Maturitas, 50*(2), 71-77.

Littner, M., Kushida, C. A., Anderson, W. M., Bailey, D., Berry, R. B., Davila, D. G., et al. (2003). Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: An update for 2002. *Sleep, 26*(3), 337-341.

Manber, R., & Bootzin, R. R. (1997). Sleep and the menstrual cycle. *Health Psychology, 16*(3), 209-214.

McHorney, C. A., Ware, J. E., Jr., & Raczek, A. E. (1993). The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical Care, 31*(3), 247-263.

Means, M. K., Edinger, J. D., & Husain, A. M. (2002). Comparison of home and laboratory actigraphy in young adults with and without primary insomnia. *Sleep, 25 (Abstract Supplement)*, A245-246.

Mendelson, W. B., Roth, T., Cassella, J., Roehrs, T., Walsh, J. K., Woods, J. H., et al. (2004). The treatment of chronic insomnia: Drug indications, chronic use and abuse liability. Summary of a 2001 New Clinical Drug Evaluation Unit meeting symposium. *Sleep Medicine Review, 8*(1), 7-17.

Merriam-Webster Inc. (1991). *Webster's ninth new collegiate dictionary*. Springfield, MA: Merriam-Webster.

Miaskowski, C., & Lee, K. A. (1999). Pain, fatigue, and sleep disturbances in oncology outpatients receiving radiation therapy for bone metastasis: A pilot study. *Journal of Pain & Symptom Management, 17*(5), 320-332.

Miller, E. H. (2004). Women and insomnia. *Clinical Cornerstone, 6*(Suppl. 1B), S8-18.

Mini Mitter Company Inc. (2003). Actiwatch activity monitors: Instruction manual (Version 3.4). Bend, OR.: Mini Mitter Company Inc.

Mock, V., Dow, K. H., Meares, C. J., Grimm, P. M., Dienemann, J. A., Haisfield-Wolfe, M. E., et al. (1997). Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncology Nursing Forum, 24*(6), 991-1000.

Mock, V., Pickett, M., Ropka, M. E., Muscari Lin, E., Stewart, K. J., Rhodes, V. A., et al. (2001). Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Practice, 9*(3), 119-127.

Moe, K. E. (2004). Hot flashes and sleep in women. *Sleep Medicine Reviews, 8*(6), 487-497.

Monk, T. H., Buysse, D. J., Kennedy, K. S., Pods, J. M., DeGrazia, J. M., & Miewald, J. M. (2003). Measuring sleep habits without using a diary: The sleep timing questionnaire. *Sleep, 26*(2), 208-212.

Monk, T. H., Reynolds, C. F., Kupfer, D. J., Buysse, D. J., Coble, P. A., Hayes, A. J., et al. (1994). The Pittsburgh Sleep Diary. *Journal of Sleep Research, 3*(2), 111-120.

Moore, R. Y. (1990). The circadian system and sleep-wake behavior. In J. Montplaisir & R. Godbout (Eds.), *Sleep and Biological Rhythms: Basic Mechanisms and Applications to Psychiatry* (pp. 3-10). Oxford: Oxford University Press.

Morgan, G. A. (2007). *SPSS for introductory statistics: Use and interpretation* (3rd ed.). Mahwah: Lawrence Erlbaum.

Morin, C. M., Hauri, P. J., Espie, C. A., Spielman, A. J., Buysse, D. J., & Bootzin, R. R. (1999). Nonpharmacologic treatment of chronic insomnia. An American Academy of Sleep Medicine review. *Sleep, 22*(8), 1134-1156.

Morin, C. M., Stone, J., Trinkle, D., Mercer, J., & Remsberg, S. (1993). Dysfunctional beliefs and attitudes about sleep among older adults with and without insomnia complaints. *Psychology and Aging, 8*(3), 463-467.

Mormont, M. C., & Levi, F. (2003). Cancer chronotherapy: Principles, applications, and perspectives. *Cancer, 97*(1), 155-169.

Moruzzi, G., & Magoun, H. W. (1995). Brain stem reticular formation and activation of the EEG. 1949. *Journal of Neuropsychiatry and Clinical Neurosciences, 7*(2), 251-267.

Mourits, M. J., Bockermann, I., de Vries, E. G., van der Zee, A. G., ten Hoor, K. A., van der Graaf, W. T., et al. (2002). Tamoxifen effects on subjective and psychosexual well-being, in a randomized breast cancer study comparing high-dose and standard-dose chemotherapy. *British Journal of Cancer, 86*(10), 1546-1550.

Munro, B. H., & Page, E. B. (1993). *Statistical methods for health care research* (2nd ed.). Philadelphia: Lippincott.

National Center for Chronic Disease Prevention and Health Promotion. (2004). *Cancer Survivorship-United States, 1971-2001*. Atlanta: CDC National Center for Chronic Disease Prevention and Health Promotion.

Neugarten, B. L., & Kraines, R. J. (1965). "Menopausal symptoms" in women of various ages. *Psychosomatic Medicine, 27*(3), 266-273.

NIH State of the Science Panel. (2005). National Institutes of Health State-of-the-Science Conference statement: Management of menopause-related symptoms. *Annals of Internal Medicine, 142*(12 Pt 1), 1003-1013.

Northouse, L. L., Caffey, M., Deichelbohrer, L., Schmidt, L., Guziatek-Trojniak, L., West, S., et al. (1999). The quality of life of African American women with breast cancer. *Research In Nursing & Health, 22*(6), 449-460.

Nunnally, J. C., & Bernstein, I. H. (1994). *Psychometric theory* (3rd ed.). New York: McGraw-Hill.

O'Connell, E. (2005). Mood, energy, cognition, and physical complaints: A mind/body approach to symptom management during the climacteric. *Journal of Obstetric, Gynecologic, and Neonatal Nursing, 34*(2), 274-279.

O'Donnell, J. F. (2004). Insomnia in cancer patients. *Clinical Cornerstone, 6*(Suppl. 1D), S6-14.

Okuyama, T., Akechi, T., Kugaya, A., Okamura, H., Imoto, S., Nakano, T., et al. (2000). Factors correlated with fatigue in disease-free breast cancer patients: Application of the Cancer Fatigue Scale. *Supportive Care in Cancer, 8*(3), 215-222.

Owen, D. C., Parker, K. P., & McGuire, D. B. (1999). Comparison of subjective sleep quality in patients with cancer and healthy subjects. *Oncology Nursing Forum, 26*(10), 1649-1651.

Owens, J. F., & Matthews, K. A. (1998). Sleep disturbance in healthy middle-aged women. *Maturitas, 30*(1), 41-50.

Parker, K. P., Kutner, N. G., Bliwise, D. L., Bailey, J. L., & Rye, D. B. (2003). Nocturnal sleep, daytime sleepiness, and quality of life in stable patients on hemodialysis. *Health and Quality of Life Outcomes, 1*(1), 68.

Pasternak, R. E., Reynolds, C. F., 3rd, Houck, P. R., Schlernitzauer, M., Buysse, D. J., Hoch, C. C., et al. (1994). Sleep in bereavement-related depression during and after pharmacotherapy with nortriptyline. *Journal of Geriatric Psychiatry and Neurology, 7*(2), 69-73.

Petit, L., Azad, N., Byszewski, A., Sarazan, F. F., & Power, B. (2003). Non-pharmacological management of primary and secondary insomnia among older people: review of assessment tools and treatments. *Age Aging, 32*(1), 19-25.

Polit, D. F., & Hungler, B. P. (1999). *Nursing research: Principles and methods* (6th ed.). Philadelphia: Lippincott.

Polo-Kantola, P., & Erkkola, R. (2004). Sleep and the menopause. *Journal of British Menopause Society, 10*(4), 145-150.

Purves, D., Augustine, G., Fitzpatrick, D., Hall, W. C., LaMantia, A. S., McNamara, J. O., et al. (2004). Sleep and wakefulness. In *Neuroscience* (3rd ed., pp. 659-685). Sunderland: Sinauer Associates.

Quesnel, C., Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2003). Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. *Journal of Consulting and Clinical Psychology, 71*(1), 189-200.

Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in general population. *Applied and Psychological Measures, 1*(1), 385-401.

Reed, P. G., Shearer, N. B. C., & Nicoll, L. H. (2004). *Perspectives on nursing theory* (4th ed.). Philadelphia: Lippincott Williams & Wilkins.

Rich, T., Innominato, P. F., Boerner, J., Mormont, M. C., Iacobelli, S., Baron, B., et al. (2005). Elevated serum cytokines correlated with altered behavior, serum cortisol rhythm, and dampened 24-hour rest-activity patterns in patients with metastatic colorectal cancer. *Clinical Cancer Research, 11*(5), 1757-1764.

Roehrs, T., & Roth, T. (2004). Sleep disorders: An overview. *Clinical Cornerstone, 6*(Suppl. 1C), S6-16.

Roscoe, J. A., Morrow, G. R., Hickok, J. T., Bushunow, P., Matteson, S., Rakita, D., et al. (2002). Temporal interrelationships among fatigue, circadian rhythm and depression in breast cancer patients undergoing chemotherapy treatment. *Supportive Care in Cancer, 10*(4), 329-336.

Rosenthal, M. B. (2003). Epidemiology, sleep, and menopause. *Menopause, 10*(1), 4-5.

Sadeh, A., Keinan, G., & Daon, K. (2004). Effects of stress on sleep: The moderating role of coping style. *Health Psychology, 23*(5), 542-545.

Sateia, M. J., & Nowell, P. D. (2004). Insomnia. *Lancet, 364*(9449), 1959-1973.

Savard, J., Davidson, J. R., Ivers, H., Quesnel, C., Rioux, D., Dupere, V., et al. (2004). The association between nocturnal hot flashes and sleep in breast cancer survivors. *Journal of Pain and Symptom Management, 27*(6), 513-522.

Savard, J., Laroche, L., Simard, S., Ivers, H., & Morin, C. M. (2003). Chronic insomnia and immune functioning. *Psychosomatic Medicine, 65*(2), 211-221.

Savard, J., & Morin, C. M. (2001). Insomnia in the context of cancer: A review of a neglected problem. *Journal of Clinical Oncology, 19*(3), 895-908.

Savard, J., Simard, S., Blanchet, J., Ivers, H., & Morin, C. M. (2001). Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. *Sleep, 24*(5), 583-590.

Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2005a). Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. *Journal of Clinical Oncology, 23*(25), 6083-6096.

Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2005b). Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part II: Immunologic effects. *Journal of Clinical Oncology, 23*(25), 6097-6106.

Savard, M. H., Savard, J., Simard, S., & Ivers, H. (2004). Empirical validation of the Insomnia Severity Index in cancer patients. *Psycho-Oncology, 14*(6), 429-441.

Scharf, M. B., McDannold, M. D., Stover, R., Zaretsky, N., & Berkowitz, D. V. (1997). Effects of estrogen replacement therapy on rates of cyclic alternating patterns and hot-flush events during sleep in postmenopausal women: A pilot study. *Clinical Therapeutics, 19*(2), 304-311.

Schiff, I., Regestein, Q., Schinfeld, J., & Ryan, K. J. (1980). Interactions of oestrogens and hours of sleep on cortisol, FSH, LH, and prolactin in hypogonadal women. *Maturitas, 2*(3), 179-183.

Schultz, P. N., Klein, M. J., Beck, M. L., Stava, C., & Sellin, R. V. (2005). Breast cancer: Relationship between menopausal symptoms, physiologic health effects of cancer treatment and physical constraints on quality of life in long-term survivors. *Journal of Clinical Nursing, 14*(2), 204-211.

Sephton, S. E., Sapolsky, R. M., Kraemer, H. C., & Spiegel, D. (2000). Diurnal cortisol rhythm as a predictor of breast cancer survival. *Journal of the National Cancer Institute, 92*(12), 994-1000.

Servaes, P., Prins, J., Verhagen, S., & Bleijenberg, G. (2002). Fatigue after breast cancer and in chronic fatigue syndrome: Similarities and differences. *Journal of Psychosomatic Research, 52*(6), 453-459.

Servaes, P., Verhagen, S., & Bleijenberg, G. (2002). Determinants of chronic fatigue in disease-free breast cancer patients: A cross-sectional study. *Annals of Oncology, 13*(4), 589-598.

Shapiro, S. L., Bootzin, R. R., Figueredo, A. J., Lopez, A. M., & Schwartz, G. E. (2003). The efficacy of mindfulness-based stress reduction in the treatment of sleep disturbance in women with breast cancer: An exploratory study. *Journal of Psychosomatic Research, 54*(1), 85-91.

Sharkey, K. M., Bearpark, H. M., Acebo, C., Millman, R. P., Cavallo, A., & Carskadon, M. A. (2003). Effects of menopausal status on sleep in midlife women. *Behavioral Sleep Medicine, 1*(2), 69-80.

Shaver, J. L., Giblin, E., & Paulsen, V. (1991). Sleep quality subtypes in midlife women. *Sleep, 14*(1), 18-23.

Shaver, J. L., & Giblin, E. C. (1989). Sleep. *Annual Review of Nursing Research, 7*(1), 71-93.

Shaver, J. L., & Zenk, S. N. (2000). Sleep disturbance in menopause. *Journal of Women's Health & Gender-Based Medicine, 9*(2), 109-118.

Shinkoda, H., Matsumoto, K., Hamasaki, J., Seo, Y. J., Park, Y. M., & Park, K. P. (1998). Evaluation of human activities and sleep-wake identification using wrist actigraphy. *Psychiatry and Clinical Neurosciences, 52*(2), 157-159.

Siegel, J. M. (2004). The neurotransmitters of sleep. *Journal of Clinical Psychiatry, 65*(Suppl. 16), 4-7.

Snyder-Halpern, R., & Verran, J. A. (1987). Instrumentation to describe subjective sleep characteristics in healthy subjects. *Research In Nursing & Health, 10*(3), 155-163.

Spelten, E. R., Verbeek, J. H., Uitterhoeve, A. L., Ansink, A. C., van der Lelie, J., de Reijke, T. M., et al. (2003). Cancer, fatigue and the return of patients to work-a prospective cohort study. *European Journal of Cancer, 39*(11), 1562-1567.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. (1983). *Manual for the State-trait anxiety inventory STAI (form Y).* Palo Alto: Consulting Psychologists Press.

Spielman, A. J., Caruso, L. S., & Glovinsky, P. B. (1987). A behavioral perspective on insomnia treatment. *Psychiatric Clinics of North America, 10*(4), 541-553.

Spielman, A. J., Nunes, J., & Glovinsky, P. B. (1996). Insomnia. *Neurologic Clinics, 14*(3), 513-543.

Stevens, R. G. (2005). Circadian disruption and breast cancer: From melatonin to clock genes. *Epidemiology, 16*(2), 254-258.

Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate statistics* (4th ed.). Boston: Allyn and Bacon.

Taheri, S. (2004). The genetics of sleep disorders. *Minerva Medica, 95*(3), 203-212.

Tatrow, K., Montgomery, G. H., Avellino, M., & Bovbjerg, D. H. (2004). Activity and sleep contribute to levels of anticipatory distress in breast surgery patients. *Behavioral Medicine, 30*(2), 85-91.

Terzano, M. G., Rossi, M., Palomba, V., Smerieri, A., & Parrino, L. (2003). New drugs for insomnia: Comparative tolerability of zopiclone, zolpidem and zaleplon. *Drug Safety, 26*(4), 261-282.

Thase, M. E. (2005). Correlates and consequences of chronic insomnia. *General Hospital Psychiatry, 27*(2), 100-112.

Thewes, B., Meiser, B., & Hickie, I. B. (2001). Psychometric properties of the Impact of Event Scale amongst women at increased risk for hereditary breast cancer. *Psycho-Oncology, 10*(6), 459-468.

Tiffin, P., Ashton, H., Marsh, R., & Kamali, F. (1995). Pharmacokinetic and pharmacodynamic responses to caffeine in poor and normal sleepers. *Psychopharmacology, 121*(4), 494-502.

Turner, J., Kelly, B., Swanson, C., Allison, R., & Wetzig, N. (2005). Psychosocial impact of newly diagnosed advanced breast cancer. *Psycho-Oncology, 14*(5), 396-407.

U.S. Bureau of the Census. (1996). *Population projections of the United States by age, sex, race, and hispanic origin: 1995-2050.* (No. P25-1130). Washington, DC.

Uchiyama, M., Okawa, M., Shibui, K., Kim, K., Tagaya, H., Kudo, Y., et al. (2000). Altered phase relation between sleep timing and core body temperature rhythm in delayed sleep phase syndrome and non-24-hour sleep-wake syndrome in humans. *Neuroscience Letters, 294*(2), 101-104.

Vena, C., Parker, K., Cunningham, M., Clark, J., & McMillan, S. (2004). Continuing education: Sleep-wake disturbances in people with cancer part I: An overview of sleep, sleep regulation, and effects of disease and treatment. *Oncology Nursing Forum, 31*(4), 735-746.

Vickberg, S. M. (2003). The Concerns About Recurrence Scale (CARS): A systematic measure of women's fears about the possibility of breast cancer recurrence. *Annals of Behavioral Medicine, 25*(1), 16-24.

Wagner, J., Wagner, M. L., & Hening, W. A. (1998). Beyond benzodiazepines: Alternative pharmacologic agents for the treatment of insomnia. *Annals of Pharmacotherapy, 32*(6), 680-691.

Walker, L. O., & Avant, K. C. (2005). *Strategies for theory construction in nursing* (4th ed.). Upper Saddle River: Pearson Prentice Hall.

Ware, J. E., Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care, 30*(6), 473-483.

Weaver, T. E., Laizner, A. M., Evans, L. K., Maislin, G., Chugh, D. K., Lyon, K., et al. (1997). An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep, 20*(10), 835-843.

Weitzner, M. A., Moncello, J., Jacobsen, P. B., & Minton, S. (2002). A pilot trial of paroxetine for the treatment of hot flashes and associated symptoms in women with breast cancer. *Journal of Pain and Symptom Management, 23*(4), 337-345.

Wilson, K. G., Watson, S. T., & Currie, S. R. (1998). Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain, 75*(1), 75-84.

You, S., Wood, P. A., Xiong, Y., Kobayashi, M., Du-Quiton, J., & Hrushesky, W. J. (2005). Daily coordination of cancer growth and circadian clock gene expression. *Breast Cancer Research & Treatment, 91*(1), 47-60.

Young, T., Rabago, D., Zgierska, A., Austin, D., & Laurel, F. (2003). Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in the Wisconsin Sleep Cohort Study. *Sleep, 26*(6), 667-672.

Zee, P. C., & Harsanyi, K. (2003). Highlights of sleep neuroscience. In T. J. Boman (Ed.), *Review of Sleep Medicine* (pp. 19-39). Boston: Butterworth & Heinemann.

CURRICULUM VITAE

Julie Lynn Elam

Education

Institution	Location	Degree/Field of Study	Date of Completion
Indiana University	Indianapolis, IN	Ph.D./Nursing	06/2008
Purdue University	W. Lafayette, IN	BSN/Nursing	05/1996
Vanderbilt University	Nashville, TN	MSN/Nursing	08/2002

Clinical Appointments

08/2003- current	Research Nurse Associate	Indiana University Indianapolis, IN
08/2002-05/2003	Research Nurse	Vanderbilt University Nashville, TN
05/2002-08/2002	Research Nurse Internship	Vanderbilt University Nashville, TN
08/2000-04/2002	Assistant Manager Oncology	Vanderbilt Oncology, Franklin TN
08/1998-08/2000	Clinical Manager Oncology	The University of Chicago Hospitals Chicago, IL
08/1997-08/1998	Nurse Associate Oncology	The University of Chicago Hospitals Chicago, IL
08/1996-08/1997	Staff Nurse Oncology	The University of Chicago Hospitals Chicago, IL

Licensure

Registered Nurse: Indiana	1996-current

Certification

Oncology Certified Nurse (OCN)	1999-current

Professional Organizations

Society of Behavioral Sleep Research	2006-current
Society for Behavioral Medicine	2005-2007
American Academy of Sleep Medicine	2005-2007
Midwest Nursing Research Society	2004-current
Purdue Nursing Alumni Organization	2003-current
President	2007-current
Member at Large	2003-2007
Member of American Society of Clinical Oncology	1999-2003
American Nurses Association	1997-current
Oncology Nurses Society	1997-current
Central Indiana Chapter: Indianapolis	2003-current
Middle Tennessee Chapter: Nashville	2000-2003
Downtown Chicago Chapter: Chicago	1999-2000
Purdue University Alumni Association	1996-current
Sigma Theta Tau Nursing Honor Society	1995-current

Volunteer

Indiana Children's Bureau Auxiliary volunteer	2003-2007
Susan Komen Race for the Cure participant/supporter	2002-2005
American Cancer Society Relay for Life	2001-2006
Leukemia Society Team in Training	1998-2004

Professional Service

Oncology Nursing Foundation Activities

Grant Review Team: Practice Change Grant-Reviewer	2004
Grant Review Team: Practice Change Grant-Reviewer	2003

Reviewer of Manuscripts

Ad-hoc reviewer with mentor, *Sleep Medicine Reviews*	2008

Honors and Awards

Educational Enhancement Grant	2008
IUPUI Outstanding Female Student Leader	2008
American Cancer Society's Career Development Conference	2007
American Cancer Society Pre-doctoral Scholarship.	2004-2008
Nursing Research Service Award: Pre-doctoral Fellowship	2006-2008
Outstanding Student Award by the Society of Behavioral Medicine	2006
Named the Mabel Burdette Pre-Doctoral Fellow- Mary Margaret Walther Cancer Institute	2005-2006
Oncology Nursing Foundation Pre-Doctoral Scholarship recipient	2005
Sigma Theta Tau Nursing Honor Society Award	1996

Biographical

Elected to the Who's Who Among Students in American Universities and Colleges

Teaching

2008 Guest Lecturer-Indiana University School of Nursing: Indiana University School of Nursing: Descriptive Research Design. Instructor: Janet S. Carpenter, PhD, RN.

2007 Teaching Assistant-Indiana University School of Nursing: Descriptive Research Design. Instructor: Janet S. Carpenter, PhD, RN.

2007 Guest Lecturer-Indiana University School of Nursing: R800 Dissertation Seminar. Instructor: Sue Rawl, PhD, RN.

2006 Guest Lecturer-Indiana University School of Nursing: R800 Dissertation Seminar. Instructor: Sue Rawl, PhD, RN.

Research and Training Grants

2006-2009 NINR 5F31NR009890-02. Predictors of sleep-wake disturbances in breast cancer survivors compared to women without cancer. (Carpenter PI, Elam Co-I) ($20,722/year direct costs)

2006-2008 American Cancer Society: Pre-Doctoral Scholarship recipient: ($30,000 per year)

2004-2005 Margaret Walther Cancer Institute: Pre-Doctoral Fellow: ($20,000 per year)

2004-2006 American Cancer Society: Pre-Doctoral Scholarship recipient: ($30,000 per year)

2004 Oncology Nursing Foundation: Pre-Doctoral Scholarship recipient: ($3,000 one time award)

2003-2004 Mary Margaret Walther Cancer Institute: Pre-Doctoral Fellow: ($20,000 per year)

Publications

Manuscripts Published (Peer Reviewed)

1. Carpenter, J. S., Storniolo, A. M., Johns, S., Monahan, P. O., Azzouz, F., Elam, J. L., Johnson, C. S., & Shelton, R. C. (2007). Randomized, double-blind, placebo-controlled crossover trials of venlafaxine for hot flashes after breast cancer. *Oncologist, 12*(1), 124-135.
2. Elam, J. L., Shu, X.O., Carpenter, J.S., Boyapati, S. & Friedmann-Gilchrist, J. (2006). Methodological Issues in the Investigation of Ginseng as an Intervention for Fatigue. *Clinical Nurse Specialist*, *20(4),* 183-186.
3. Carpenter, J. S., Elam, J. L., Ridner, S. H., Carney, P. H., Cherry, G. J., & Cucullu, H. L. (2002). Sleep, fatigue and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. *Oncology Nursing Forum, 31(3),* 591-598.

Book Chapters

1. Carpenter, J. S., & Elam, J. L. (2003). Menopausal symptoms (Chapter 16). In K. H. Dow (Ed.). *Contemporary Issues in Breast Cancer (2nd Ed.).* Boston: Jones and Bartlett.

Presentations

Abstracts

Poster Presentations

1. Elam, J.L., Carpenter, J.S., Russell, K., & Champion, V. (accepted 03/10/08). Severity of sleep disturbances in long-term breast cancer survivors. 2008 International Menopause Society Conference, Madrid, Spain.
2. Elam, J. L., Carpenter, J. S., Russell, K. M. & Champion, V. L. Prevalence of sleep disturbances in BCS. American Academy of Sleep Medicine's 22nd Annual Sleep Conference, Baltimore, MD, June 2008.
3. Elam, J. L. Why do breast cancer survivors have trouble sleeping? 1st Annual Graduate Education Day. Indiana State Capital, March, 2008.
4. Elam, J. L., Carpenter, J.S., Shu, Xiao-Ou, Boyapati, S., and Gilchrist, J. Ginseng for the Treatment of Fatigue in Breast Cancer. Accepted for poster presentation. ONS National Conference on Cancer Nursing Research, Hollywood, CA, February 7-9, 2007.
5. Carpenter, J. S., Elam, J. L., Printy, J., Lemler, S., & COBRA. Methodological considerations in developing and implementing a multi-site hot flash core. ONS National Conference on Cancer Nursing Research, Hollywood, CA, February 7-9, 2007.
6. Elam, J. L. & Carpenter, J. S. (2005). Daily Variability in Wrist Actigraphy in Breast Cancer Survivors Experiencing Hot Flashes. American Academy of Sleep Medicine's 20th Annual Sleep Conference, Salt Lake City, Utah, June 19-22, 2006.
7. Elam, J. L. & Carpenter, J. S. (2005). Predictors of sleep-wake in breast cancer survivors with hot flashes. Society of Behavioral Medicine's 27th Annual Meeting and Scientific Sessions, San Francisco, CA, March 22-25.
8. Elam, J. L. & Carpenter, J. S. (2005). Evaluation of Subjective Sleep for Breast Cancer Survivors Experiencing Hot Flashes. Midwest Nursing Research Society's 29th Annual Research Conference, March 2005.
9. Elam, J. L. & Carpenter, J. S. (2005). Relationships Among Objective Sleep Parameters, Objective Hot Flashes, and Subjective Hot Flashes in Breast Cancer Survivors. Poster presentation: 8th National Research Conference on Cancer Nursing Research: Ft. Lauderdale, FL.
10. Elam, J. L. & Carpenter, J. S. (2004). Results of Pittsburgh Sleep Quality Index Parameters for Female Breast Cancer Survivors Seeking Treatment for Hot Flashes. Poster presentation: Indiana University Cancer Center 2nd Annual Cancer Research Day, Indianapolis, IN.
11. Elam, J. L. & Carpenter, J. S. (2004). Results of Pittsburgh Sleep Quality Index Parameters for Female Breast Cancer Survivors Seeking Treatment for Hot Flashes. Poster presentation: 30th Annual Nursing Research Conference: Indianapolis, IN.

12. Elam, J. L. & Carpenter, J. S. (2004). Results of Pittsburgh Sleep Quality Index Parameters for Female Breast Cancer Survivors Seeking Treatment for Hot Flashes. Poster presentation: 15th International Research Congress, Dublin, IR.

Podium Presentations

1. Elam, J. L. (2003). Sleep, fatigue, and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. Late breaking abstract #58, podium presentation at 28th Annual Oncology Nursing Society Congress, Denver, CO.